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NEURITIS SYPHILITICA OF THE OLFACTORY NERVE

REPORT OF A CASE

Leopold Liss, M.D.

Ann Arbor, Mich.

Syphilitic meningo-encephalitis sometimes affects the optic nerve and produces syphilitic optic neuritis. The clinical symptomatology as well as the pathological picture are well known. The opticus and the olfactorius are in a unique position among other cranial nerves because they represent extracerebral prolongations of cerebral tracts; they show much greater resemblance to the brain in the normal histological picture and in different pathological sequelae.

It is not surprising that neuritis on a syphilitic basis may occur in the olfactory nerve, although to our knowledge there are no previous descriptions in the literature of neuritis olfactoria syphilitica.

REPORT OF A CASE

The patient, an 80 year old male, was hospitalized in various hospitals and mental institutions with a confirmed clinical diagnosis of central nervous system syphilis. His mental symptoms consisted of confusion, disorderly behavior, memory loss and delusions of grandeur. The examination of serum and spinal fluid was positive for

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From the Laboratory of Neuropathology, Department of Psychiatry, University of Michigan Medical School, Ann Arbor, Michigan.

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lues. On physical examination the respiratory system was carefully described: no nasal discharge or obstruction was noted; the septum was found in the midline; the turbinates were of normal size and the mucosa was of normal appearance. The function of the first nerve was not examined.

Autopsy Findings. The brain was reduced in size; the blood vessels showed minimal arteriosclerotic changes; the meninges were thickened and opaque. The olfactory bulbs and nerves were greatly reduced in size and adherent to the meninges. The measurements of the olfactory bulbs were 2.5 x 1.0 mm, which represent an approximate two-thirds loss.

Materials and Methods. The olfactory nerves were carefully removed and after fixation in brom-formalin (Cajal's solution) they were cut on freezing microtome at 15 microns and impregnated with variants of the silver-carbonate technique described by Scharenberg and Zeman.[1]

Description of Material. The olfactory bulb does not show any of the normal histological structures and definition of the different layers is not possible (Fig. 1). The tissue of the olfactory bulb is very cellular and is composed mostly of astroglial elements. Around the blood vessels the perivascular glial elements and connective tissue are increased in number. In the olfactory bulb there are present peculiar whorl formations of cellular elements. One of these whorl-formations is present in the tip of the olfactory bulb (Fig. 1) and the majority of these cells can be identified as fibrocytes with only few astroglial elements scattered around (Fig. 2). Figures 3 and 4 show the posterior portion of the olfactory bulb and on the periphery of the bulb several dense whorl-formations, which under higher magnification reveal about equal amount of fibrocytes and astroglia. Similar structures can be found in the anterior portion of the olfactory tract (Fig. 5). (Although the exact demarcation between the bulb and the tract is arbitrary since the cytoarchitecture of the bulb is destroyed, the line is thought to be where the anterior portion narrows.) The whorls in the olfactory tract are less dense than those in the bulb and are formed almost exclusively of astrocytes with only few fibrocytes among them (Fig. 6). Along the olfactory tract there are many areas which appear less dense than others (Fig. 7). They represent loose astroglial scar formations (Fig. 8), with an increased cell population along the border of the lesion and are formed by proliferated astrocytes with large bodies and numerous thick processes (Fig. 9). In the olfactory bulb no normal ganglion

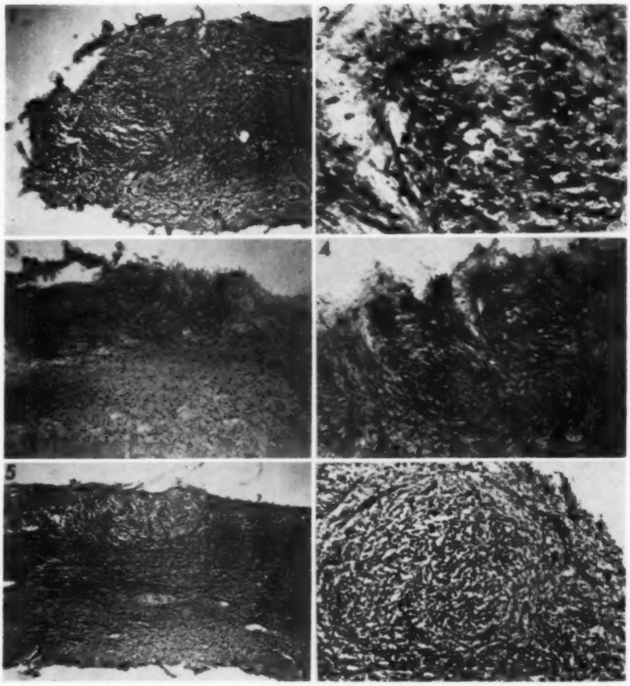


Fig. 1.—Tip of the olfactory bulb. There is complete absence of normal cytoarchitecture. Whorl-shaped scar formation in the anterior portion. Photomicrograph. Zeiss Neofluar 6,3 X.

Fig. 2.—Scar formation from Figure 1. Numerous fibrocytic elements with few scattered astrocytes. Photomicrograph. Zeiss Neofluar, 40 X.

Fig. 3.—Olfactory bulb. Several whorl-shaped scars in the periphery of the bulb. Photomicrograph. Zeiss Neofluar, 6,3 X.

Fig. 4.—Same area as in Figure 3. In the scar formation are present fibrocytes and astrocytes. Photomicrograph. Zeiss Neofluar, 16 X.

Fig. 5.—Anterior portion of the olfactory bulb. On the periphery a loose scar formation is present. Photomicrograph. Zeiss Neofluar, 6,3 X.

Fig. 6.—High magnification of one of the whorls shown in Figure 5. The scar is formed predominantly by astrocytes with only few fibrocytic elements. Photomicrograph. Zeiss Neofluar, 16 X.

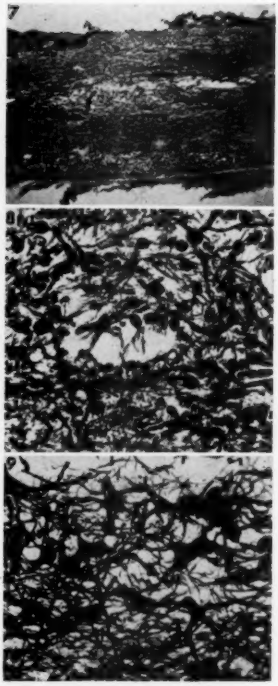


Fig. 7.—Olfactory tract. Loose scar formation is present in the central portion of the tract. Photomicrograph. Zeiss Neofluar, 6,3 X.

Fig. 8.—Same area as Figure 7. Loose astroglial scar with moderate oligodendroglial activity. Photomicrograph. Zeiss Neofluar, 40 X.

Fig. 9.—Same area as Figure 7. Border of the lesion. The astroglial elements are proliferated, have large bodies and long, thick processes. Photomicrogarph. Zeiss Neofluar, 40 X.

cell layer was found, just an occasional neuron or a cluster of ganglion cells. The majority of these neurons are severely degenerated, their processes are swollen and fragmented and they are surrounded by numerous glial elements (Fig. 10). In some areas around fairly well preserved neurons, an abundance of glial elements is distinguishable (Fig. 11); these cellular accumulations represent a recent reaction in which numerous microglial elements appear as gitter cells, the oligodendroglia are swollen and the astroglia severely degenerated with fragmentation and disintegration of the processes (klasmatodendrosis) (Figs. 12 and 13).

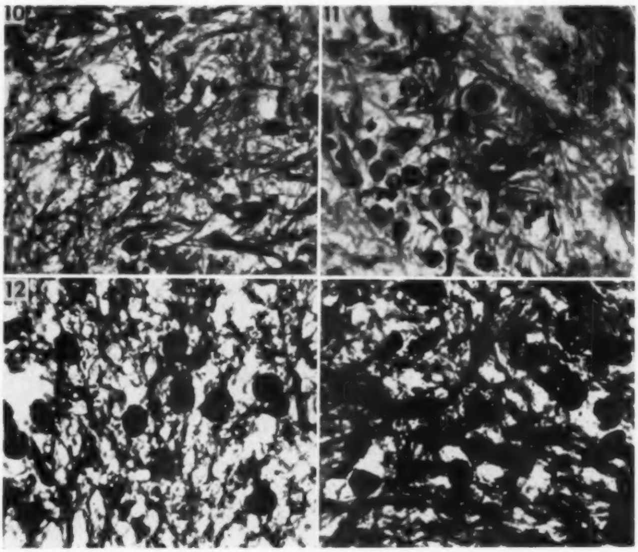


Fig. 10.—Olfactory bulb. Degenerated nerve cells with moderate glial activity around them. Photomicrograph. Zeiss Neofluar, 40 X.

Fig. 11.—Olfactory bulb. Fairly well preserved neuron (arrow) located close to a blood vessel is surrounded by numerous glial elements, mostly swollen oligodendroglia and gitter cells. Photomicrograph. Zeiss Neofluar, 40 X.

Figs. 12 and 13.—Olfactory bulb. Gliosis which represents an active pathological process. The cells are gitter cells, swollen oligodendroglia, and astrocytes with klasmatodendrosis. Photomicrograph. Zeiss Neofluar, 80 X.

The reduction in number of neurons in the olfactory bulb and their degeneration is followed by markedly reduced amount of the nerve fibers in the central portion of the bulb (layer of the olfactory nerve fibers) and in the olfactory tract. The meninges which cover the olfactory tract are adherent and markedly thickened. This thickening of the meninges is caused by the proliferation of thick layers of the connective tissue which covers the tract. There is no cellular activity in the meninges (Fig. 14).

Some of the nerve fibers in the olfactory tract show thickenings and bulbs of degeneration (Cajal's[2] bulbs) (Fig. 15). The amyloid bodies are rarely scattered among the nerve fibers. The paucity of the nerve fibers and low cellular population of the olfactory tract

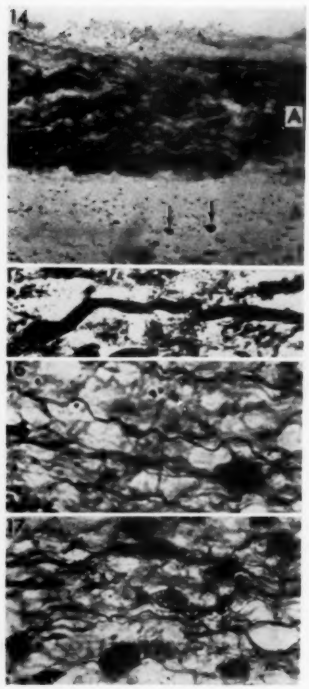


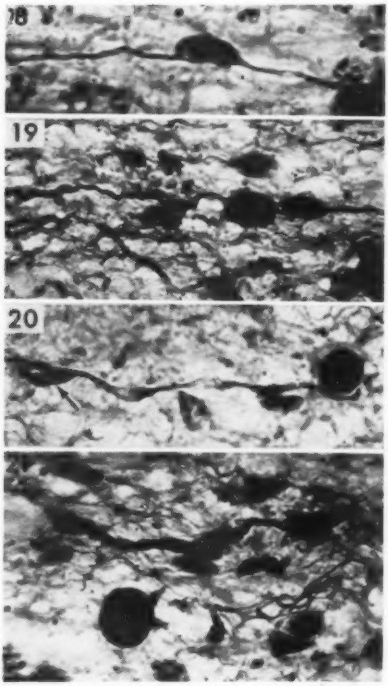
Fig. 14.—Olfactory tract. Thick meninges (A) cover the tract (B) in which few cellular elements and nerve fibers are visible. Also few amyloid bodies can be recognized (arrows). Photomicrograph. Zeiss Neofluar, 6,3 X.

Fig. 15.—Olfactory tract. Thickened nerve fiber with end-bulb or degeneration. Photomicrograph. Zeiss Neofluar, 100 X.

Fig. 16.—Olfactory tract. Normal Schwann element with spindle shaped body and two long processes. Photomicrograph. Zeiss Neofluar, 100 X.

Fig. 17.—Olfactory tract. Swollen element of Schwann located close to a degenerated nerve fiber. Photomicrograph. Zeiss Neofluar, 100 X.

permit a very careful analysis of the amyloid bodies. Figure 16 shows few nerve fibers, a Schwann element with a spindle shaped body and two long processes (Fig. 16.). Other perineural elements which support an apparently damaged nerve fiber are slightly swollen (Fig. 17). The bodies of the Schwann elements become enlarged and their large processes indistinguishably fused with the nerve fiber (Fig. 18); eventually they become almost spherical (Fig. 19). In the most progressed stage of degeneration the cells completely lose



Figs. 18-21.—Olfactory bulb. Stages of gradual transformation of swollen and degenerated Schwann elements into amyloid bodies. Photomicrograph. Zeiss Neofluar, 100 X.

their characteristics and appear as darkly impregnated spherical bodies close to the nerve fiber (Fig. 20). Another Schwann element close to this nerve fiber (Fig 20 arrow) is slightly degenerated but still can be recognized as a cell. The amyloid bodies in the olfactory tract are present only among the nerve fibers and none were found around the blood vessels. Frequently the nerve fibers are swollen and fragmented (Fig. 21).

COMMENT

In this case of central nervous system syphilis the olfactory bulb and nerve were grossly atrophic. None of the normal structures were present:[3] there are no fibers of the fila olfactoria (first layer),

and no glomeruli are present (second layer); the third (ganglionic) layer is represented by more or less damaged neurons which are found either singly or in clusters but their number is extremely reduced. Consequently in the layer of the olfactory nerve fibers (fourth layer) only few nerve fibers are present. Numerous scars formed by fibrocytes and astrocytes are present in the bulb and in the tract. They represent old lesions in which no trace of the originally present structures is left. These lesions are similar to the scar formations found in other parts of the nervous system after complete destruction of the normal structures. Besides areas which have been destroyed before, there is still evidence of progressing degeneration. The damaged neurons surrounded by micro- and oligodendroglia with evidence of klasmatodendrosis show that the destructive process is still in progress although not much of the normal cytoarchitecture is left.

This picture of degeneration and repair is different from the one found in the olfactory nerve in neuromyelitis optica;[4] although the nature of the process is inflammatory, the chronic character is much more pronounced. This is characterized by solid scarification on one side and active degeneration on the other. Since in the other areas of the nervous system only very minimal changes were found, it is difficult to establish correlation between the changes in the olfactory nerve and in the rest of the nervous system.

We have attempted to compare the changes in the olfactory with those in syphilitic optic nerve atrophy. Although syphilis may affect all cranial nerves, this is due to syphilitic meningitis and always accompanied with very pronounced findings in the meninges and in the brain.[5] The already-mentioned histological relationship between the opticus and olfactory as well as the fact that optic atrophy, although mostly associated with tabes, may be present in absence of other symptoms in the nervous system[6] shows close correlation between this case and the well known picture of syphilitic optic atrophy. We consider the present case an extremely chronic and latent form of primary neuritis which affects not only the tract but the olfactory bulb as well (similar to the neuroretinitis).[7] The still active degenerative changes are not accompanied in our case with the typical patho-anatomical picture of neurosyphilis, but the brain also disclosed only minimal histological findings associated with a definite psychiatric picture of tertiary syphilis.

The primary difficulty in classification of the type of syphilitic involvement of the olfactory bulb and nerve lies in the fact that we do not know the time in which the patient had anosmia since the

examination of the first nerve is frequently omitted as was the case in the described patient. With complete destruction of the first two layers of the olfactory bulb and only few nerve cells and fibers remaining, the sense of smell was obviously lost. The presence of any disease in the nose with secondary degeneration of the olfactory nerve can be eliminated as well by the histological picture as by the detailed rhinoscopic examination.

Amyloid bodies are very low in number and their distribution is different to those found in cases when the olfactory atrophy is secondary to the degeneration of the nasal mucosa.[8] This finding gives a new importance to the amyloid bodies which are considered an unspecific product of degeneration of the various structures of the nervous system. The amyloid bodies were described as final products of degeneration of neurons, nerve fibers[9] and astroglia. In the present case the majority is an end product of degeneration of the Schwann elements. The astroglia in the described case plays an active part in the formation of scar tissue and shows very little activity around the vessels, thus leaving these areas which, in cases of secondary and senile degeneration of the olfactory nerve are filled with amyloid bodies, almost free. The amyloid bodies in the present case are found among the degenerated nerve fibers.

SUMMARY

Almost complete degeneration of the olfactory bulbs and tracts was found in a patient with syphilis of the central nervous system. The changes consisted of peculiar scar formations, and degeneration of perineural elements of Schwann which produced amyloid bodies.

UNIVERSITY HOSPITAL

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XLVI

STUDIES IN SIALOLITHIASIS

I. THE STRUCTURE AND MINERALOGICAL COMPOSITION OF SALIVARY GLAND CALCULI

IRVING M. BLATT, M.D.

REYNOLDS M. DENNING, PH.D.

JAMES H. ZUMBERGE, PH.D.

AND

JAMES H. MAXWELL, M.D.

ANN ARBOR, MICH.

In this study of the structural characteristics and composition of salivary calculi, the disciplines of the geologist, mineralogist and micro-analytical chemist have been applied.

Analyses of 30 salivary calculi from 21 patients are presented. The great majority of this group occur singly. The size of the calculi vary from 1 mm in circumference and 2 mm in length to 1.7 cm by 3.0 cm (Fig. 1). The calculus found in the hilum of the salivary gland is usually larger than the duct calculus. The hilar calculus is usually spherical or oval, while the one from the duct is elongated and resembles a date-pit (Fig. 2). An amorphous, yellowish to brown resinous material covers the surface. The resinous material surrounding the hilar calculus is thickly applied, imparting a rind-like appearance. The hilar calculus usually has an irregular, knobby, colloform surface (Fig. 3), whereas the surface of the usually smaller duct calculus is finely granular. No faceted surfaces are present in this collection.

INTERNAL STRUCTURE

A study of the structure of a salivary gland calculus is best accomplished by carefully fracturing the stone across its long axis

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From the Departments of Otolaryngology, Mineralogy and Geology, University of Michigan, Ann Arbor.

This study was aided by the Walter L. Hill Medical Research Fund.

TABLE I

DISTRIBUTION AND SIZE OF SALIVARY CALCULI IN THIS STUDY

PATIENT	AGE	NUMBER OF STONES	SIZE	SOURCE
A.G.	65	4	each 1 mm in diameter	submaxillary salivary gland
J.W.	26	2	2 mm x 4 mm 2.5 mm x 7.5 mm	submaxillary salivary gland
A.S.	29	2	6 mm x 7 mm 3 mm x 4 mm	submaxillary salivary gland
H.K.	49	2	1.5 mm x 3 mm 5 mm x 7.5 mm	submaxillary salivary gland
H.S.	48	1	9 mm x 11.5 mm	submaxillary salivary gland
B.W.	56	1	5 mm x 7 mm	submaxillary salivary gland
R.T.	23	1	6 mm x 9 mm	submaxillary salivary gland
E.L.	38	1	3 mm x 8 mm	submaxillary salivary gland
H.J.	52	1	8.5 mm x 12.5 mm	submaxillary salivary gland
E.B.	33	1	9.5 mm x 14 mm	submaxillary salivary gland
J.P.	65	1	17 mm x 30 mm	submaxillary salivary gland
J.C.P.	39	1	7.5 mm x 12 mm	submaxillary salivary gland
N.S.	20	1	5 mm x 7.5 mm	submaxillary salivary gland
K.H.	22	1	4 mm x 7.5 mm	submaxillary salivary gland
H.U.	52	1	7.5 mm x 10 mm	submaxillary salivary gland
E.B.	42	1	10.5 mm x 20 mm	submaxillary salivary gland
I.N.	49	1	6 mm x 9 mm	submaxillary salivary gland
D.H.	35	4	each 1 mm in diameter	parotid salivary gland
G.D.	44	1	4.5 mm x 7.5 mm	parotid salivary gland
C.F.	24	1	2 mm x 3.5 mm	parotid salivary gland
J.W.	36	1	1 mm x 1.5 mm	parotid salivary gland

TOTAL: 21 Patients 30 Stones

Comprehensive tables on x-ray diffraction spacing data, which accompanied the manuscript but are not printed, are available from the authors to readers specially interested.

after it is firmly mounted in beeswax. Fracture of the calculus permits inspection of such structural characteristics as lamination, porosity, texture and the study of individual crystals; and is necessary if the nucleus is to be observed and analyzed. The split specimens may be remounted in beeswax for stereoscopic microscopy or embedded in clear plastic and polished for photographing. Samples of material can then be removed for examination under the polarizing microscope or by x-ray diffraction.

Fig. 1.—Representatvie apatite calculi from the parotid and submaxillary salivary glands.

The Laminated Structure. The salivary calculus of either parotid or submaxillary gland origin is definitely laminated. Concentric shells of a white chalky substance are clearly visible between layers of brownish-yellow resinous material (Fig. 4). The layers of white chalky material may be of equal size or thicker than its resinous counterpart. Of the two varieties, the latter is the most common accretionary configuration. It would appear that the alternating light and dark bands represent stages of growth about a single orb or nucleus. However, careful dissections of the various calculi in this collection also reveal a single specimen containing several small circular orbs which suggests that growth may sometimes begin not around a single center but around two or more. As growth continues, however, the enclosing layers of white material coalesce and a single larger calculus appears as the final product. The outermost covering of all the stones in this series is composed of the aforementioned resinous material.

The Nucleus. Because most laminated structures suggest a nucleus around which accretion begins, all the calculi of this collection were examined carefully under the high powered binocular dissection microscope (20x). Except for the purposes of photographing the cross section which requires that a stone be fractured through the

sagittal plane, most of the calculi were dissected in toto. During the dissection it again becomes evident that each calculus is formed by accretion of material, layer upon layer. The laminated pattern becomes less conspicuous as the central core is approached and finally disappears when the nucleus is isolated. The central core appears as a single spheroid mass (Fig. 5); it is of chalky white color, texture and porosity that characterizes the white material from the various stony shells previously removed. The nuclei vary from 0.5 to 1.5 mm in diameter.

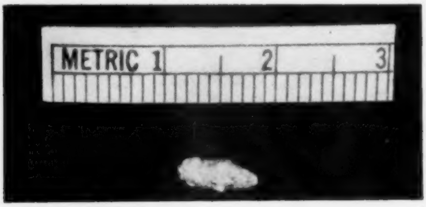

Fig. 2.—A submaxillary (Wharton's) duct calculus from case E.L. The duct calculus is frequently elongated and resembles a date pit. The surface is finely granular.

When the nucleus is fragmented, it appears completely structureless and without recognizable features. In order to determine the presence of a foreign body or other recognizable material, the nucleus of each calculus was crushed between two glass plates (Fig. 6). The plates can be bound tightly with porous binding and sealed in one corner. The specimens can then be stained with Gram's stain, Wright's stain, Zeihl-Neilsen and methylene blue for identification of cellular material or micro-organisms; or examined unstained with ordinary reflected light. So far as can be determined from this type of examination, no foreign body or organism or other microscopically recognized material is visible, even after the slide sandwich is opened and the open faces examined under oil immersion.

Possible Growth Stages. The laminated pattern of a calculus, besides revealing its morphological character, indicates its pattern of growth. The inference from the salivary calculus is that the physicochemical relationship during growth alternates between an environment causing accretion of a calcareous substance with periods favoring the accumulation of an outer rind of resinous material (Fig. 4). Just what initiates or localizes the first stage of accretion is not

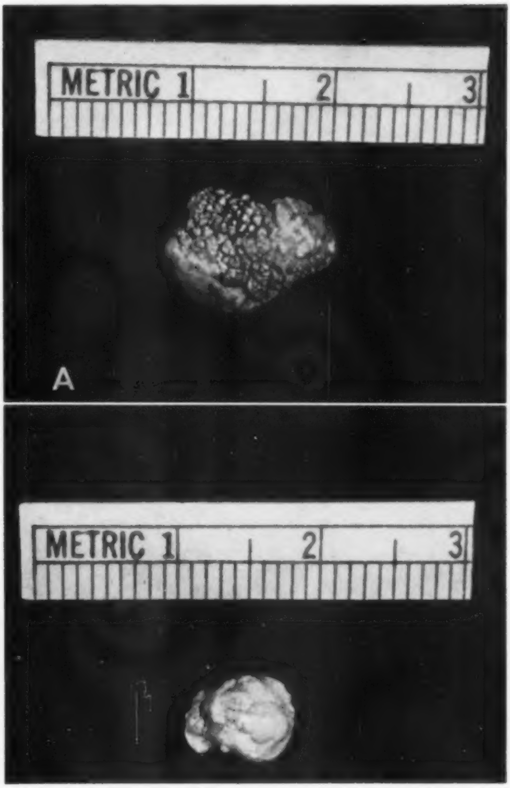

Fig. 3.—(A) Calculus from case H.J. found in the hilum of the submaxillary salivary gland. The hilar calculus usually has an irregular, knobby colloform surface. (B) The smooth surface calculus is a common variant.

explainable from this study. But once accretion commences, it appears to continue in a pulsating manner with periods of rapid accretion (white material) separated by intervals of little or no enlargement characterized by accumulation of yellow-brown rind.

ANALYSIS BY METHODS OF OPTICAL AND X-RAY CRYSTALOGRAPHY

The mineral nature of salivary calculi has suggested the application of the techniques of mineralogy to the identification of the

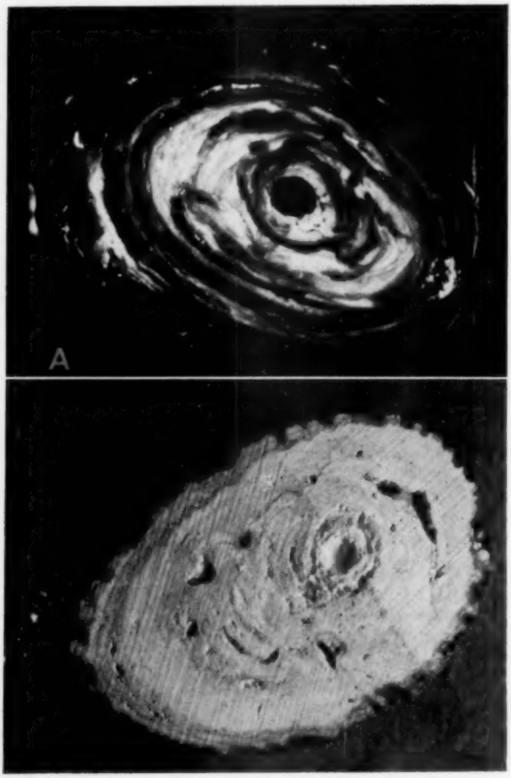

Fig. 4.—(A) A macrophotograph (19 x enlarged) of the cross section of a parotid gland calculus (case G.D.). The specimen was embedded in clear plastic and polished for photographing by the reflected light technique. The laminated structure of a salivary gland calculus is visible. The white material alternates with the darker bands which in actual color are yellow-brown and possess a resinous luster. The plane of the section is not through the exact center of the innermost core or nucleus. (B) Section of submaxillary gland stone from case J.P. (4 x enlarged).

crystalline components of salivary calculi. The well recognized physical methods of polarizing (petrographic) microscopy[1] and x-ray diffraction[2] have therefore been applied to the study of salivary calculi.

Analysis by Optical Methods. It is well known that chemical compounds tend to form crystals when they pass from the liquid to

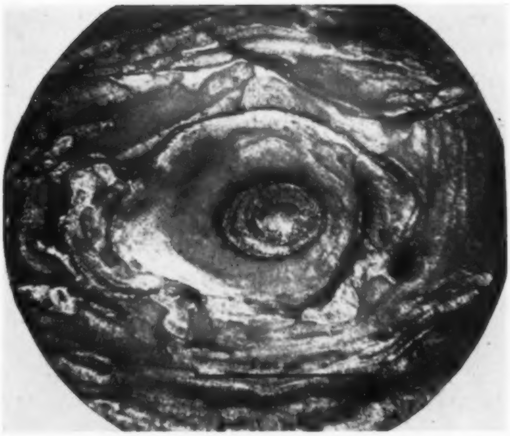

Fig. 5.—Photomicrograph (40 x) of the central part of the parotid calculus from case G.D.

the solid state. The external geometric form and the internal atomic arrangement of such crystals are distinct, constant and characteristic for any particular substance. Even when conditions in the environment are unfavorable for the development of visible geometrical crystal faces, the seemingly amorphou crystalline mass has the same internal atomic structure.

As light passes through transparent crystalline material, it is influenced by the crystal structure according to the laws of optics. These changes in transmitted light are accurately measurable, which provide data called optical constants. Having determined the optical constants of a series of compounds of known chemical composition, it is possible to recognize unknown substances by measuring their optical constants and comparing these data with prepared tables. In practice the calculus is fractured and examined grossly as previously described. A sample is then crushed, placed on a glass slide, immersed in suitable liquids of known index of refraction, and examined with the petrographic microscope. The index (or indices) of refraction is measured by selecting a liquid of matching index of refraction. Another useful determinative constant, birefrigence, may be estimated from interference colors observed between crossed polars. The details of the theory and techniques of such determinations are described in the standard mineralogical references.[3,4]

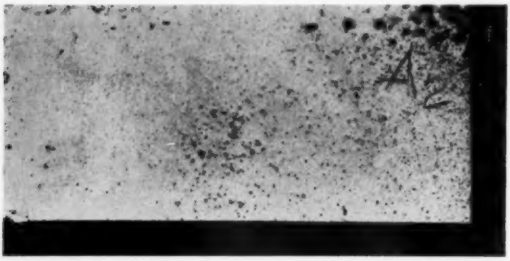

Fig. 6.—Nucleus from a submaxillary salivary gland stone (case A.G.) crushed between two glass plates for determination of foreign bodies, or other recognizable material or organisms (4 x enlarged).

Examination by X-ray Diffraction. The x-ray technique used in the analysis of salivary calculi is the powder method of Hull or of Debye and Scherrer.[3] It is well known that the solid crystalline substances consist of atoms arranged in an orderly three dimensional pattern. This arrangement of atoms in planes is illustrated in Figure 7 which shows the structure of a crystal of sodium chloride ($NaCl$). In utilizing the powder method, a finely powdered sample of a substance is irradiated by a beam of monochromatic x-rays. The rays are reflected at certain angles which depend upon the interplanar spacings and the wave length of the x-rays. The x-rays are recorded as a series of lines upon a cylindrical photographic film, forming a characteristic pattern for the substance irradiated (Fig. 8). The intensity of the lines as well as their spacings are characteristic.

Since no two chemical compounds have precisely identical crystal structures, the x-ray diffraction patterns by which their structural characteristics are revealed are unique and offer the most reliable means of identification. The mineralogist frequently terms these patterns the "finger prints of the crystals." The powder patterns can be applied in several ways for the purposes of identification. In one method the spacings of the lines on the films are measured and the interplanar spacings are calculated for the substance in question. The spacings are given in ångstrom units ($1\ \text{Å} = 10^{-8}$cm) or the nearly identical x-units. Comparison is then made with a tabulated list of interplanar spacings of known chemical substances. In addition to the spacings, the relative intensities of the lines on the film is specified on a scale of one to zero or ten to zero. Often for determinative work a visual estimate of intensity is satisfactory. Terms such as strong (s), medium (m), weak (w), and very weak (vw) are

frequently used. Intensities are purely relative for the pattern of one substance and cannot be used to compare the intensities of lines in one pattern with those of another. A published list of interplanar spacings is available from the American Society for Testing Materials.[5,6] Identification of a powder pattern may also be achieved by direct comparison of the unknown patterns with standard x-ray patterns of known substances. Spacing data together with reproductions of powder patterns are given in this study for the known constituents of salivary deposits.

The size of the sample required for an x-ray diffraction powder study is quite small. A convenient size is a few milligrams, but 1 mg or less will suffice. When dealing with mixtures it is possible to identify the several constituents and to estimate the approximate proportions of each by the relative intensities of the superimposed patterns.

CHEMICAL ANALYSIS OF SALIVARY CALCULI

While it is true that modern physical methods of mineralogic identification are quite accurate, it is advisable to check these physical tests by chemical examination. Minerals are naturally occurring homogeneous substances of a more or less definite chemical composition. The chemical composition is variable within certain limits. This variation is due to the random substitution of one ion in a crystal structure by another ion of a similar size. Such substitution is termed isomorphism or solid solution. Often only a small amount of the substituting ion is present. For such cases the x-ray diffraction pattern may not exhibit a measurable difference from the pattern of the ideal pure mineral. In general the effect of such isomorphism is to change slightly the spacings of lines on the x-ray film and to modify their relative intensities by a small amount.[23,24]

The analytical methods of inorganic chemistry can be applied not only for the identification of ideally pure minerals, but for the detection of small amounts of ions that may be present in isomorphous substitution. The qualitative micro-analytical procedures for salivary calculi analysis have also been used in this study of gall bladder[7] and urinary stones.[8-10]

APPLICATION OF THE ANALYTICAL METHODS

The Crystalline Component of Salivary Calculi. The methods of optical and x-ray crystallography and qualitative microchemical

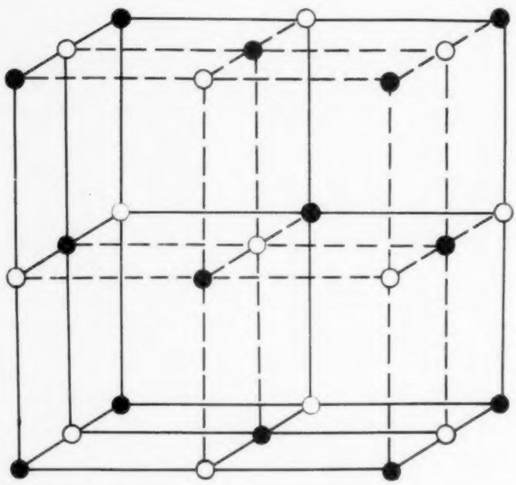

Fig. 7.—Structure of NaCl. Solid spheres represent sodium atoms and the hollow ones chlorine atoms (or vice versa). Arrangement of the atoms in planes is well illustrated.

analysis as applied to this collection of salivary stones reveal only one distinct crystalline substance to be present: Carbonate-apatite, $CaCO_3(Ca_3(PO_4)2)x$. This substance is a complex carbonated calcium phosphate which can be identified only by optical or x-ray methods.

The term apatite refers to a group of complex phosphate compounds which have an analogous chemical composition and nearly identical crystal structure. The following apatites occur biologically and form an isomorphous series of minerals capable of solid solution in one another:[15]

1. Carbonate-apatite, $CaCO_3(Ca_3(PO_4)_2)x$
2. Hydroxyapatite, $Ca(OH)_2(Ca_3(PO_4)_2)x$
3. Fluorapatite, $CaF_2(Ca_3(PO_4)_2)x$
4. Chlorapatite, $CaCl_2(Ca_3(PO_4)_2)x$
5. Oxyapatite, $CaO(Ca_3(PO_4)_2)x$

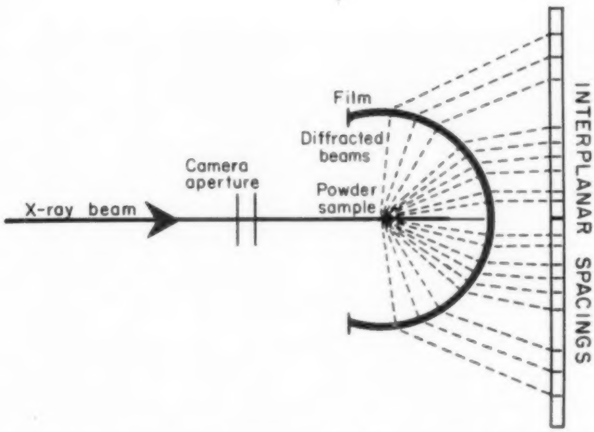

Fig. 8.—A diagrammatic illustration of the method used to obtain x-ray diffraction (powder) photographs.

Carbonate-apatite and hydroxyapatite occur in urinary calculi[11,12] and in gall stones.[7] Carbonate-apatite is the principal constituent of calcifications variously formed in the lacrymal duct, prostate gland, tuberculous lymph nodes, appendix, testes and the walls of the bronchi as a consequence of senile degeneration and disease as shown by Frondel and Prien.[13] All five of the above apatites have also been described as being constituents of bone,[14] enamel and dentin.[15] The individual apatites can be identified by optical or x-ray methods under ideal conditions. However, their differentiation by powder patterns per se is difficult. This difficulty is enhanced because of the possibility of isomorphism. On the other hand, they may be differentiated by various microchemical qualitative tests which will be described in this paper.

Optical Data. Apatite is hexagonal in crystallization, but well formed crystals are found only in inorganic nature. It has a hardness of 5 on the Mohs scale and a specific gravity of 2.95 to 3.10. The natural crystals are optically negative, with O and E indices in the range from 1.61 to 1.64, depending on the kind and amount of isomorphous substitution.

Apatite in this collection of salivary calculi is found as irregular fine grains with a banded spherulitic structure. The various samples are practically isotropic and the index varies between 1.55 to 1.59.[16]

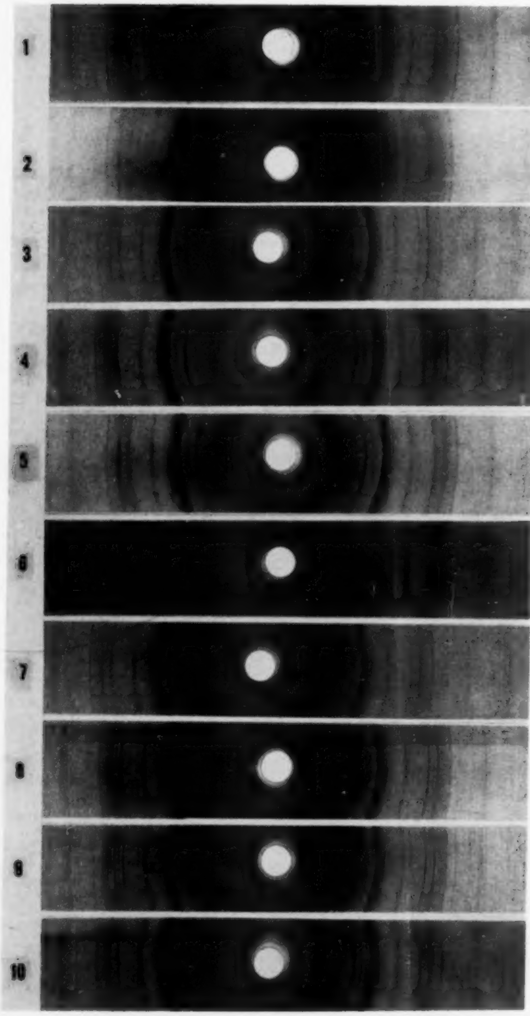

Fig. 9.—X-ray diffraction (powder) photographs of the crystalline apatite mineral found in 8 salivary gland calculi representative of this collection. Patterns 1 through 8 correspond with the spacing data for the cases as enumerated in Table II. The last 2 patterns are of known standard carbonate-apatite (pattern 9) and hydroxy-apatite (pattern 10).

The isotropic or nearly isotropic character is due to the small size of the crystals, their inherent low birefrigence, and the random orientation of the aggregate of submicroscopic crystals. The variation in index is probably due to variation in the content of adsorbed water and capillary water.

X-ray Diffraction Data. The various samples give a distinct x-ray powder pattern of apatite. Direct comparison of our unknown patterns with the diffraction pattern of known carbonate apatite show both to be identical. Figure 9 shows the powder patterns of 8 salivary calculi. All show a typical apatite pattern. Characteristically, the lines are rather diffuse, although in one example the lines are fairly sharp. The characteristic lack of sharpness is due either to the very small size of the crystals or to a low degree of perfection of crystallization. The last two patterns are of known-standard carbonate-apatite (pattern 9) and hydroxyapatite (pattern 10).

The interplanar x-ray spacing data indicate that there are no other substances present which can be identified by this physical method with the possible exception of about one per cent calcite ($CaCO_3$) in one stone (case H.K.). It would therefore appear that the crystalline material in this salivary calculi collection is virtually pure apatite.

Prien and Frondel,[17] in a study of 700 urinary calculi stated, "Pure apatite calculi are not very common; they are fine-grained, soft and compact in structure. Ordinarily there is concentric lamination, both on a microscopic and macroscopic scale. . . . Pure apatite may exist in alternating laminations of white and brown in which the brown layers represent a condensation of the substance. The brown layers may be translucent or even transparent." This description fits exactly the 30 salivary calculi in this collection. However, the brown shells in this group of salivary stones, by gross and microscopic morphological examination in no way resemble a crystalline substance, but an organic, amorphous material.

In order to substantiate our morphological impression, the brown resinous shells were submitted to x-ray diffraction analysis. In preparation of such a sample for examination, it is extremely difficult to remove every grain of the white apatite material without subjecting the sample to dissolution of any unknown pigmented crystalline material by strong acids.

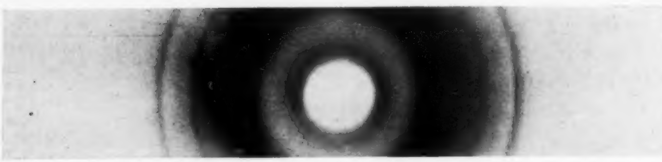

Fig. 10.—X-ray diffraction analysis of organic, resinous material dissected from the various dark laminations of a salivary gland calculus. Particles of calcareous material where adherent since they could not be removed without altering the composition of the sample. This accounts for the very weak apatite pattern on the film. The general configuration of the film, however, is characteristic of amorphous substances, particularly the strong broad "halo" observed at the low angle of 17°. The spacing data are given below:

d (Å)	I	d (Å)	I	d (Å)	I
5.2	br str H	2.15	vvw(d)	traces	?
3.44	m str	2.05	wtr?(d)	1.455	wtr
2.80	str	1.95	vw	some	
2.71	vvw	1.89	vvw(d)	additional	
2.63	vvw	1.84	w	possible	
2.27	vvw(d)	1.72	w	traces	

SYMBOLS: br = broad, str = strong, H = halo, m = moderate, w = weak, v = very, tr = trace, ________ = sharpest lines, (d) = most diffuse lines, ? = questionable.

The x-ray diffraction pattern of a yellow-brown shell of a salivary calculus is not characteristic of apatite which has become yellow or brown due to a content of foreign pigmented matter. A strong broad halo is observed at the low 2 Θ angle of about 17 degrees. Such diffraction patterns are generally characteristic of amorphous substances, although patterns of this kind are seen in finely divided and poorly crystallized clays. Poorly crystallized materials which produce the diffraction halo usually show additional more sharply resolved diffraction lines characteristic of the pattern of the respective materials. The remainder of our pattern of a salivary calculus sample corresponds with apatite but the lines are weak, diffuse and incomplete (Fig. 10). This probably represents the small amount of white material which cannot be removed from the resinous shell without altering the composition of the sample.

Microchemical Analysis. X-ray diffraction analysis of a substance present in a given sample shows the true state of chemical

composition. The analysis is conclusive, even though only minute amounts of material are available. Identity of minor constituents can therefore be readily accomplished. The substance is analyzed directly in its "as received" state and is not altered or destroyed.

However, x-ray diffraction analysis is a method limited to solid substances which are crystalline, meaning by crystalline those substances which give a pattern. As little as one per cent of a minor constituent can be detected, although many would not show at less than ten per cent.[5] The magnitude of this figure can be estimated only after the pattern has been obtained but cannot be foretold beforehand. Another factor to be considered is that an appreciable percentage of elements may be present in solid solution without changing the pattern sufficiently to be detected, at least without special techniques. Thus, while certainty of x-ray diffraction is one of the valuable features of the method, this certitude applies only to what the powder pattern does show and not to what it does not show. For these reasons the x-ray data are not independent and therefore must be combined with other data for complete information.

Chemical analysis[18] has therefore been applied and has provided a valuable adjunct to this investigation. Since the various apatites mentioned are usually identified as apatite by optical or x-ray methods, the various microchemical qualitative analytical tests can be applied for more specific identification of the apatites.

The Carbonate in Carbonate-Apatite, $CaCO_3(Ca_3(PO_4)_2)x$. A few grains of the sample are placed upon a glass microscopic slide and covered with a cover slip. A drop of dilute hydrochloric acid, HCl, is then run under the edge of the cover glass. If carbonate-apatite is present an effervescence ensues which may be watched through low power magnification. If there is doubt that the bubbles consist of carbon dioxide, CO_2, rather than displaced air, a drop of barium hydroxide, $Ba(OH)_2$, solution may be introduced underneath the cover slip. As the barium hydroxide diffuses through the acid underneath the cover glass, a white precipitate of barium carbonate, $BaCO_3$, will form about the salivary stone material, thus showing the presence of CO_2. If a drop of one normal nitric acid, HNO_3, is then added, the CO_2 can be seen to bubble a second time. All 30 specimens in this collection gave a positive reaction as described.

Failure to produce effervescence may be considered to indicate the presence of hydroxyapatite, $Ca(OH)_2(Ca_3(PO_4)_2)x$. Fluor-

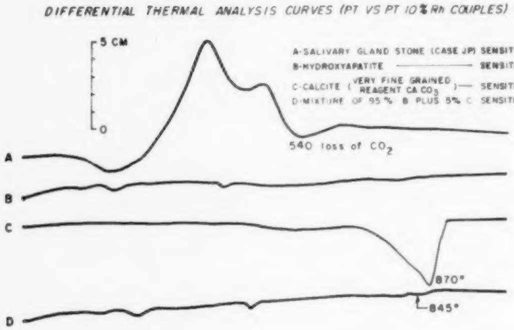

Fig. 11.—The study of a carbonate apatite salivary gland calculus by differential thermal analysis (D.T.A.). Curve A (stone from case J.P.) indicates that calcite, $CaCO_3$, was not detected. The carbonate (CO_3) was liberated as CO_2, probably at 540° C., a reaction quite different from that of calcite (curve C). The upward deflections (exothermic reactions) in curve A are probably due to oxidation of the organic matter in the stone.

apatite, $CaF_2(Ca_3(PO_4)_2)x$, and chlorapatite, $CaCl_2(Ca_3(PO_4)_2)x$, will not effervesce with HCl and will not give precipitation with barium hydroxide, $Ba(OH_2)$, since barium fluoride, BaF_2, and barium chloride, $BaCl_2$, are both soluble.

The Fluoride in Fluorapatite, $CaF_2(Ca_3(PO_4)_2)x$. A small quantity of the sample is dissolved in concentrated sulphuric acid, H_2SO_4, in a watch glass coated with paraffin; slots down to the glass are made in the paraffin. Evolution of hydrofluoric acid, HF, which etches glass indicates the presence of fluoride. Because of the small size of some of the calculi in this collection, only 23 stones were so tested. No positive reaction for fluoride was obtained in the calculi studied. A specimen of fluorapatite tested in the described manner yielded a good fluorine test in 10 minutes.

The Chloride in Chlorapatite, $CaCl_2(Ca_3(PO_4)_2)x$. In a chloride solution (small quantity of the sample dissolved in dilute nitric acid, HNO_3), silver nitrate, $AgNO_3$, gives a white curdy precipitate which is soluble in ammonium hydroxide, NH_4OH. No positive reaction for chloride was obtainable in 23 stones analyzed for halides.

The necessity for a simple yet accurate method by which naturally occurring concretions could be qualitatively analyzed, prompted

investigators in the physical and biological sciences[8-10] to use the above-described and other chemical tests. On the basis of these determinations, certain supposed constituents of salivary calculi recorded in the literature[19,20] are found to be non-existent when sought for by physical methods of identification. This points up the weakness of chemical analysis of salivary calculi per se, for this method, too, is not independent.

Phosphates. Chemical analysis of salivary calculi is generally reported as showing "per cent of calcium phosphate" and "per cent of calcium carbonate.[19,25]" This was undoubtedly due to the lack of understanding of the true nature of the crystalline substance or substances that might have been present. The presence of phosphate can be easily determined chemically by standard analytical tests for this acid radical. However, ultimately it is not possible by chemical tests alone to determine if the phosphate is: 1) an apatite (complex phosphate), 2) magnesium ammonium phosphate hexahydrate, $MgNH_4PO_4 \cdot 6H_2O$, 3) calcium hydrogen phosphate dihydrate, $CaHPO_4 \cdot 2H_2O$, 4) tricalcium phosphate, $Ca_3(PO_4)_2$, or any combination of the last three—all of which have been described in disease states.[11,13,17] We have failed to identify any of the last three phosphates mentioned in this collection of salivary calculi.

Magnesium Ammonium Phosphate Hexahydrate, $MgNH_4PO_4 \cdot 6H_2O$. This substance is generally associated with apatite in urinary calculi in fairly large concentration.[17] Its mineralogical name is struvite. A urinary calculus which contains struvite is characteristically columnar in structure. When associated with apatite, a so-called "stag horn" renal calculus is formed. Such a calculus is dirty to creamy white and the columnar or cellular structure resembles cancellous bone. The intercolumnar spaces of the stag horn struvite calculus is usually filled with apatite. This is in distinct contrast to the solid, shell-like laminations of a salivary gland calcuus. The x-ray powder pattern of struvite is characteristic and is easily distinguished from that of apatite. Magnesium ammonium phosphate hexahydrate is orthorhombic-hemimorphic in crystal form. Under the microscope it is easily distinguished by its crystal form, birefrigence, and low indices of refraction. Small quantities of magnesium in a sample of calculus can be detected microchemically. The sample is dissolved in dilute hydrochloric acid, and a solution of ammonium chloride is added. The test solution should be cold. Ammonium hydroxide is then added to make the solution alkaline. When disodium hydrogen phosphate, Na_2HPO_4, is added, $MgNH_4PO_4 \cdot 6H_2O$,

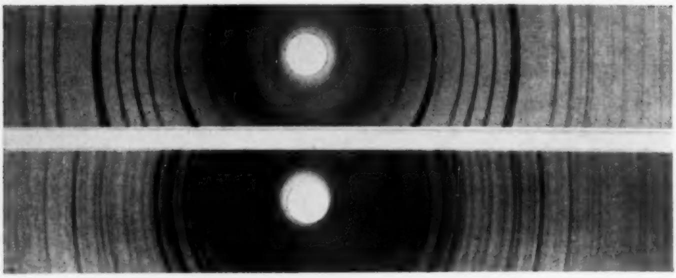

Fig. 12.—X-ray diffraction (powder) photographs of known standard calcite (top picture) and whitlockite (bottom picture).

microscopic struvite is formed which is easily identified under the microscope.

Calcium Carbonate, $CaCO_3$. As previously mentioned, the development of effervescence when a calcareous stone is treated with dilute acid is evidence only for the occurrence of the carbonate (CO_3) radical. This is due to the presence of either calcium carbonate (as the mineral calcite) or carbonate apatite; or both. Calcium carbonate is commonly reported to occur in salivary calculi[19,20] as determined by chemical analysis. However, in this study it was found only in one instance (Case H.K.) with the approximate concentration of one per cent, as determined by physical methods. In the investigations on urinary calculi by Jensen,[11] and Prien and Frondel[17] who also used the physical methods of identification, calcium carbonate was not found. Thus, it would appear that the development of effervescence, in practically all instances in this study, was due to the presence of carbonate apatite.

ADDITIONAL STUDY BY DIFFERENTIAL THERMAL ANALYSIS

One sample (stone from case J.P.) was subjected to a differential thermal analysis (D.T.A.)[21] in an attempt to demonstrate the occurrence of calcite ($CaCO_3$) by an additional sensitive method. This particular sample was selected since the other stones were too small for such a study. In this method, a sample is heated simultaneously with a thermally inert material. Thermocouples in the sample and in the inert reference material are connected to a recorder so that

the temperature difference between the unknown and the reference material is plotted against time. Exothermic reactions are indicated by an upward deflection and endothermic reactions are manifest by a downward deflection. The temperature at which various reactions occur are also recorded (Fig. 11).

An x-ray powder pattern of the heat-treated stone from case J.P. was made in order to study any possible deviation from the pattern of the untreated material. The following substances were studied by D.T.A. by heating at 12° C. to 1000° C.:

1. The unknown: A sample of stone from case J.P.

2. Control A.: Hydroxyapatite.

3. Control B.: Calcite - very fine grained reagent $CaCO_3$ (Fig. 12 and Table III).

4. A mixture of 95% hydroxyapatite (2) and 5% calcite (3).

Four observations are quite significant in this experiment. 1) The D.T.A. data indicate that calcite was not detected (Fig. 11) unless it co-existed with apatite in an amount no greater than 0.5% to 1.0%—a level below which this method is not sensitive under the experimental conditions.[22] 2) The x-ray diffraction pattern of apatite in stone J.P. was sharpened to a marked degree after heating, and a number of new phases including the mineral whitlockite (tricalcium phosphate, $Ca_3(PO_4)_2$) were developed (Fig. 13). Thus some of the apatite, $R(Ca_3(PO_4)_2)x$, must have been transformed into whitlockite as a result of rearrangement of atoms during heating. The carbonate (CO_3) was liberated as CO_2 probably at 540° C., a reaction which was quite different from that of calcite (Fig. 10, Line C). 3) When the heated sample (stone J.P.) was treated with dilute acid (HCl) for the development of effervescence, none occurred. Thus, it would appear that the loss of carbonate was not due to the breakdown of calcite, but due to the loss of carbonate in the apatite (Fig. 10). 4) The upward deflections (exothermic reactions—Fig. 10, Line A) are probably due to oxidation of the organic matter in the stone (resinous shells of protein material).

Also, the above observations, when coupled with the spacing data of the standard carbonate apatite and hydroxy apatite powder patterns, strengthens our observation that the distinction of the specific apatites from one another as they occur biologically is most difficult

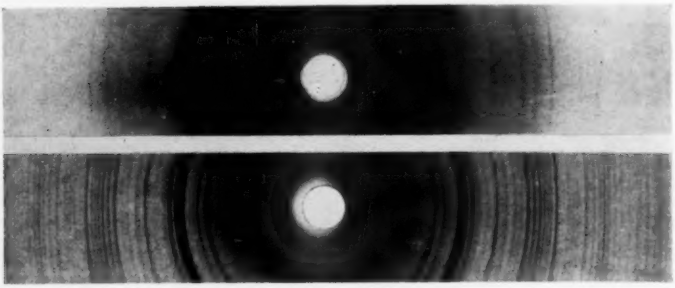

Fig. 13.—X-ray diffraction (powder) photographs of submaxillary salivary gland calculus from Case J.P. before (top picture) and after (bottom picture) differential thermal analysis. The post D.T.A. diffraction pattern of apatite was sharpened to a marked degree and a number of new phases including the mineral whitlockite ($Ca_3(PO_4)_2$-tricalcium phosphate) were developed. Some of the apatite, $R(Ca_3(PO_4)_2)x$, must have been transformed into whitlockite as a result of rearrangement of atoms during heating.

by either optical examination or x-ray diffraction alone or specifically by chemical analysis. These methods supplement each other.

THE PROBLEM OF WHITLOCKITE IN SALIVARY GLAND CALCULI

In 1946 Frondel and Prien[13] identified carbonate apatite as the only crystalline constituent in salivary gland calculi by the x-ray diffraction method. A similar study by Jensen and Danø[26] in 1952 revealed not only apatite but whitlockite (tricalcium phosphate, $Ca_3(PO_4)_2$) as well. This is of considerable interest since this mineral was detected in the identical manner as we have encountered it in this investigation, by x-ray diffraction analysis of heat-treated stone specimens. This further substantiates our observation that the presence of whitlockite (Fig. 12) is an artifact of a thermal reaction which alters the atomic structure of apatite.

SUMMARY AND CONCLUSIONS

1. The primary objectives of this investigation have been to seek accurate knowledge concerning the structure and exact composition of the crystalline constituents of the salivary gland calculus. The

methods of the geologist, mineralogist and micro-analytical chemist have been applied to the development of a practical procedure to accomplish these aims.

2. The salivary gland calculus has a laminated structure. Concentric shells of the calcareous mineral, apatite, alternate with layers of organic, brownish-yellow resinous material which also form the outer covering of the stone.

3. The central core or nucleus is a single spheroid mass, composed of apatite. It appears completely structureless and without recognizable features. No foreign organism or inert foreign body was recovered from the nuclei of the 30 salivary calculi examined.

4. The laminaed pattern of the salivary calculus indicates its pattern of growth. The inference is that the physicochemical relationship during growth alternates between an environment causing accretion of a calcareous substance with periods favoring the accumulation of an outer rind of organic, resinous material. Just what initiates or localizes the first stage of accretion is not explainable from this study.

5. The crystalline component of a salivary gland calculus is practically pure apatite, as determined by optical, x-ray and microchemical techniques. The term apatite refers to a group of biologically occurring complex phosphate compounds which have an analogous chemical composition and nearly identical crystal structure. Carbonate-apatite appears to be the apatite in the salivary gland calculus. As determined by other investigators,[26] approximately one per cent of calcite is sometimes associated with carbonate bearing apatites. Differential thermal analysis (D.T.A.) has been used to further verify our results.

6. It must be remembered that the data presented are based on only 30 specimens. Studies including a larger number of samples are necessary to corroborate these findings.

University Hospital

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Dr. Blatt's present address is Hauser Clinic, 7411 Third Avenue, Detroit 2, Mich.

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XLVII

NICOTINE STOMATITIS OF THE PALATE

WILLIAM H. SAUNDERS, M.D.

COLUMBUS, OHIO

That tobacco smoke causes definite lesions in the hard palate is a well documented fact. Dental pathologists and oral surgeons write occasionally describing this interesting group of oral lesions and call them "nicotine stomatitis" or "papular leukoplakia," but I have been unable to find similar references in otolaryngological literature. Patients with mild degrees of nicotine stomatitis are frequently seen, but as with many other conditions, if the examiner is not thinking of this disorder and is not looking for it, he fails to recognize it and considers it rare. On the other hand, advanced stages of nicotine stomatitis are usually not overlooked but are often misdiagnosed.

In the oral cavity, nicotine and its combustion products produce pathological changes chiefly in the hard palate. Tobacco smoke probably strikes the palate more directly than other parts of the oral cavity. It may also be that the hard palate is especially sensitive to tobacco smoke. Classically, the pipe smoker is said to be most prone to develop nicotine stomatitis, but today cigarette smokers seem to account for most instances.

Patients who chew tobacco and hold their wad in one particular place sometimes develop white plaque-like areas of hyperkeratosis or leukoplakia on the gingiva and buccal mucosa. Pipe smokers may develop leukoplakia or carcinoma of the lip. These conditions are not considered here.

The drawings which illustrate this article are accurate representations of color photographs. These lesions are even better appreciated when seen in color. For that reason I wish to direct the attention of the interested reader to the excellent photographs of nicotine stomatitis found in *The Color Atlas of Oral Pathology*.

CLINICAL APPEARANCES

When one examines the normal palate using a bright light, tiny orifices of mucous glands are visible. These normal duct orifices are seen as small depressions and usually are whiter than the surrounding mucosa. Sometimes the normal duct opening may look slightly pink. Although the same glands are present in the soft palate their orifices are not apparent.

The mucosa of the hard palate is tightly applied to bone. As a result the soft tissue of the hard palate is thinner and less vascular than the soft palate. This color distinction seems important because an exaggeration of this difference marks most instances of nicotine stomatitis.

1. *The Common Lesion* (Figs. 1 and 2). In the most common type of nicotine stomatitis, the orifices of mucous glands become red while the surrounding mucosa remains normal or is slightly blanched. Such lesions, repeated many times throughout the posterior two-thirds of the palatal mucosa, produce a pattern of tiny red dots against a background of normal or somewhat pale mucosa. The dots vary in size but generally they are about 0.5 mm in diameter. The lesions are located posteriorly in the palate because there are more glands posteriorly than anteriorly.

2. *Papular Lesion*. Rather rarely, a patient is seen in whom the appearance of the common lesion is greatly exaggerated. The red dot of the common lesion becomes an umbilicated center for the papule of grey mucosa (Fig. 3). The papule is firm and not tender and the lesions are multiple. Some authors call the condition "papular leukoplakia" (due to nicotine).

Figure 4 shows two or three large papules and many smaller papules against a background of markedly thickened epithelium which is raised into tiny ridges.

3. *Ulcerative Lesion*. Even more unusual than the papular lesion is the ulcerative lesion of nicotine stomatitis. Biopsies of such an ulcer and its margin demonstrate granulation tissue and chronic inflammation without evidence of neoplasm or specific granuloma. These lesions are not very painful unless severely infected.

The ulcer shown in Figure 5 was treated unsuccessfully with various medicaments including antibiotics, and with cautery. It

Fig. 1.—*The Common Lesion.* A drawing slightly exaggerating a lesion in the hard palate of a smoker with a moderate degree of nicotine stomatitis. Similar but less marked changes may be seen in many heavy smokers.

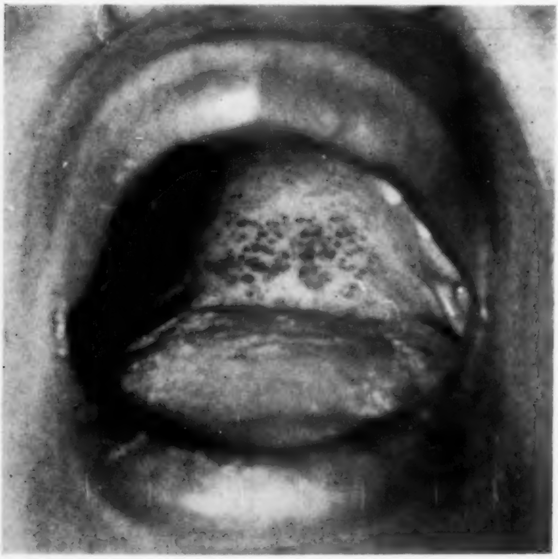

Fig. 2.—An advanced stage of the common macular lesion in a woman.

Fig. 3.—*Papular Lesion.* Called "papular leukoplakia" by some authors, this lesion is much less common than that seen in Figure 1.

Fig. 4.—Several papular lesions are seen along with dry thickened epithelium.

Fig. 5.—*Ulcerative Lesion.* Ulcer of the palate believed to be due to smoking.

Fig. 6.—*Ulcerative Lesion.* Deep ulcer of palate believed to be due to smoking. The white center is a slough.

Fig. 7.—Same lesion as in Figure 6, healing. The only treatment given was to stop smoking and use of saline irrigations. Repeated biopsies and cultures in vitro and in vivo were "negative."

healed promptly, and without other treatment, only when the patient stopped smoking.

Figure 6 is a photograph of the palate of a very heavy smoker with a great destructive, painful ulcer. Several large biopsies were taken to establish a suspected diagnosis of carcinoma but the pathologist never was able to confirm the clinician's suspicion of malignancy. Instead the pathologist continued to report "chronic, non-specific inflammatory reaction." Cultures of the material removed by biopsy failed to grow bacterial or yeast agents ordinarily capable of producing such necrosis. The serologic test for syphilis was negative, as were all other customery laboratory examinations.

This ulcer started to heal promptly (Fig. 7) and continued to show healing during several weeks when the patient used saline irrigations and stopped smoking. Before complete healing of the lesion the patient left town and could not be contacted for a final photograph.

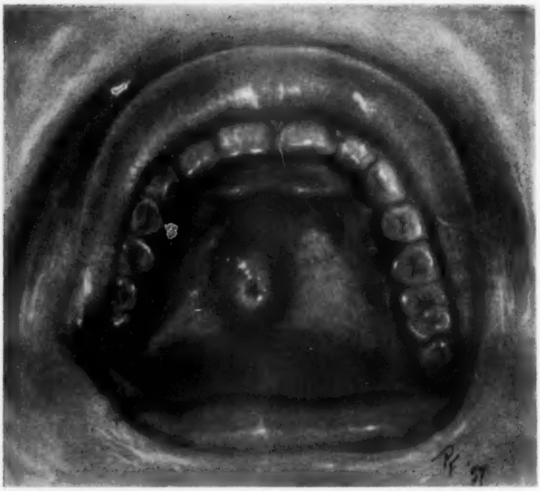

Fig. 8.—*Granulomatous Lesion.* Note the blanching of the adjacent mucosa. In the hard palate smoking produces a whiteness and in the soft palate, a redness.

Fig. 9.—*Granulomatous Lesion.* Sometimes these furrows become very deep and are secondarily infected.

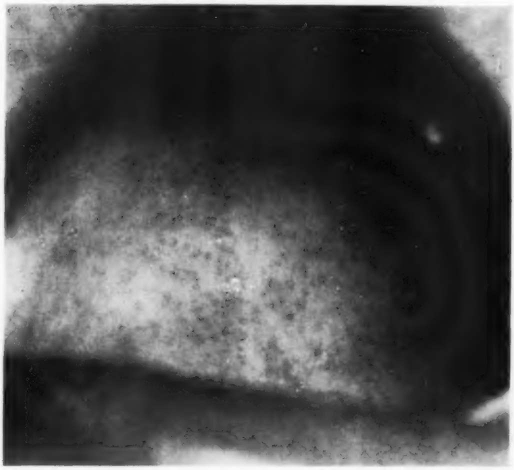

Fig. 10.—*Soft Palate Lesion.* On close inspection dilated vessels are seen. Throughout the soft palate are pink papillary projections.

This may be another example of palatal disease due to smoking, but, so far as I know, ulcerative lesions of the palate due to smoking have not been reported before. Therefore the reader is cautioned to weigh this part of the report carefully. After all, there is no laboratory test which can prove that a particular oral lesion is caused by smoking. However, my personal clinical judgment is that the ulcerative lesions shown here were caused by smoking.

Earlier writers describing nicotine stomatitis mention that it is possible to produce palatal lesions by having a non-smoker use tobacco. I have been able to confirm this observation readily. One can produce the common macular lesion by having a non-smoker use a package of cigarettes daily for a week or two. Small red dots appear in the palate and then clear shortly when smoking is stopped. Or, in the case of the heavy smoker, the palate improves after several weeks of non-smoking.

4. *Granulomatous Lesion.* Figure 8, illustrating another advanced lesion of nicotine stomatitis, shows a large granuloma with a central depression. The adjacent mucosa is very blanched. The palate looks as if it were trying to form a boil or extrude a foreign

body. The patient eventually healed this lesion when he stopped smoking.

Other granulomatous lesions of nicotine stomatitis may produce deep vertical rugae and furrows in the palate (Fig. 9). The palate is hyperemic and may be painful because of secondary infection. The furrows and ridges appear to be exaggerations of normal palatal irregularities observed in some patients.

5. *The Soft Palate Lesion.* This is fairly common but again the condition is easily overlooked. There is a fine, pink, wartline or papillary formation over much of the soft palate mucosa (Fig. 10). Although the palate feels slightly rough the patient does not complain (he cannot feel his soft palate with his tongue). This is the only discrete type of lesion I have seen involving the soft palate which can be reasonably attributed to smoking.

Smoking also causes a hyperemia of the soft palate. Sometimes one sees a network of fine vessels scattered over the soft palate and uvula. At other times distinct vessels are not made out but there is an over-all redness. These appearances are common to most smokers. In fact it is so common that the doctor may forget that it is not normal. Smoking tends to cause the hard palate to become blanched and the soft palate reddish so that the normal color difference between the hard and soft palates is accentuated.

THE SYMPTOMS

Except for ulcerative and large granulomatous lesions nicotine stomatitis is virtually asymptomatic. An occasional patient with a papular lesion may say that he can feel a roughness of the palate with the tip of his tongue but most patients do not complain unless their attention is directed to the condition by a doctor.

(Heavy smokers sometimes notice a sandpaperlike or pebblelike roughness when feeling the floor of the mouth with the tip of the tongue. This sensation, caused by dilatation of mucous glands, is not associated with visible disease. Biopsies of the tissue have shown only very active mucous glands and ducts filled with mucus.)

THE PATHOLOGY

The microscopic appearances of nicotine stomatitis vary depending on the stage of disease. Early, there is an increase in the keratin

layer of the epithelium. This accounts for the white or grey mucosa. Later, when papule formations occur, there is a dilatation of the ducts of mucous glands and tissue infiltration with lymphocytes. The duct lining may undergo metaplasia to squamous epithelium and some of the ducts become obstructed by desquamated epithelium. Excellent photomicrographs have been published in articles by Thoma[2] and Cummer.[3]

THE TREATMENT

Nicotine stomatitis clears only when the patient stops smoking. Then the lesions disappear and symptoms, if any, subside. Some authors recommend the fitting of a denture for the inveterate smoker who refuses to renounce his habit.

An occasional patient may have the disease so advanced that the doctor is compelled to take a biopsy to rule out malignancy. Oral surgeons sometimes strip a part of the palatal mucosa where frank leukoplakia is present. I am not aware of published papers describing the occurrence of carcinoma of the palate as a result of smoking.

UNIVERSITY HOSPITAL

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XLVIII

SOME PRINCIPLES OF VESTIBULAR HYDROMECHANICS

JUERGEN TONNDORF, M.D.

AND

WILLIAM A. VAN BERGEIJK, PH.D.

IOWA CITY, IOWA

The mechanics of cupular reaction in the semicircular canals has not received much attention of late in contrast to its close phylogenetic relative, the cochlea. Our understanding of the auditory function of the ear has been greatly improved since Bekesy started, 30 years ago, his investigations of the mechanical properties of the ear. His approach included direct measurement of structural properties, experimentation on human and animal ears, and the use of models. Bekesy once expressed his concept of the significance of analog or model experimentation in a discussion remark to a paper by one of the present authors. He was referring to the complexity of the traveling wave phenomenon in the cochlea and continued: ". . . Therefore the only thing that I could do and somebody else could do for the moment is to do the next thing, do experiments. If you do an experiment you can first work with analogies. You can make some similar systems and then you can make a real model. . . . After I make the dimensional model, then I take a guinea pig and see if I can find in the guinea pig's ear the same thing; going this way back and forth, it is possible to establish many facts and many problems in a much clearer and simpler way because I can separate them. . . ."

The present writers decided to look into the basic mechanical properties of the semicircular canals from a similar viewpoint, using simple mechanical models. The results of such studies should provide a better point of departure for the understanding of more complex phenomena actually observed in laboratory animals or in man.

There are two important points which have been argued pro and con for a long time in the past concerning the mechanical prop-

erties of the semicircular canals. Both of them have been settled in a satisfactory manner for some time. 1) The experiments by Steinhausen[8] on the labyrinth of the pike have demonstrated that the cupula actually deflects in response to a movement of the endolymph. 2) Observations under the phase microscope by several observers have established the fact that the cupula in the living state extends to the roof of the membraneous ampulla, presumably making a reasonably good seal.

With experimental and clinical data available in 1931 Schmaltz treated the problem mathematically and came to the following conclusions: A semicircular canal during rotatory stimulation in its own plane performs a differentiation between the speed of the osseous (and the membranous) canal walls and that of the endolymph so that this relative speed is directly proportional to the acceleration (positive or negative) the canal is undergoing. More exactly the acceleration is proportional to the relative speed times a constant. This constant is made up by the opposing inertial and frictional forces, i.e., by the dimensions of the canal and the density and viscosity of the endolymph. Since frictional damping is high, the onset period (the time until the system reaches a steady state) is approximately 0.02 sec. which is brief in terms of the duration of rotatory motions of the human body or the head alone. From this we may conclude that the cupula obtains quantitative information concerning the angular acceleration of the head by detecting the velocity of the endolymphatic fluid occurring at any given time relative to that of the osseous canal walls. The shortness of the transitional periods at the beginning and at the end of each motion aids in this task.

The present writers limited the scope of their investigation to obtaining some general information: the factors governing what might be called the dynamic range of the cupular response; the effects of the driving force and the flow resistance on cupular deflection; and finally, the effects of flow direction. No attempt was made in this study to obtain quantitative data which are directly applicable to the vestibular organs of animals or of man, the interest being limited to the establishment of general functional relations.

The following mechanical circuit was used (Fig. 1a). A small glass tank representing the utricle was connected in series to a glass tube containing the cupula. A small pump (with a manometer in parallel) was used to generate a driving force. The input to the pump was also connected to the tank, thus representing the small crus of the semicircular canal. Connection between the various com-

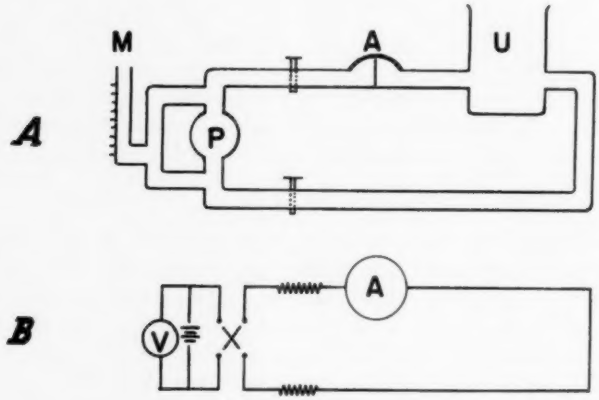

Fig. 1.—A: Schematic diagram of the semicircular canal model. U: utricle; A: ampule; P: pump; M: manometer in parallel with the pump. Flow resistance was regulated at the two places indicated.
B: Electrical analog of the above.

ponents was by short pieces of rubber tubing. The resistance in this closed system was regulated at two places: in the small crus, and in the ampullated crus between the pump and the cupula. Both ampullo-petal and ampullo-fugal flow directions were used. For the sake of comparison, the diagram of an analog electrical circuit is added (Fig. 1b). Since no attention was paid to the on- and off-phenomena, the proper viscosity of the fluid was neglected and tap water was used as endolymphatic fluid in all experiments. Flow rate was measured as the time needed for a standard amount of fluid to pass through the pump. For graphing purposes the values were converted into the conventional expression of cc/min.

The first item investigated concerned the factors governing the dynamic range of cupular reaction. The cupula, represented by a small flap of rubber, extended from its mounting into the glass tube, almost touching the walls all around the periphery. First a straight piece of tubing (cf. insert of Fig. 2) was used and thereafter a dome-shaped ampulla, its outer periphery being a circular segment with the cupular mounting at the inner periphery and about at the center of this circle. As can be seen from Figure 2, there was a significant difference between the two cases in the function relating flow rate and deflection. In the case of the straight tube, this function was nonlinear almost from its onset, gradually approaching a ceiling value

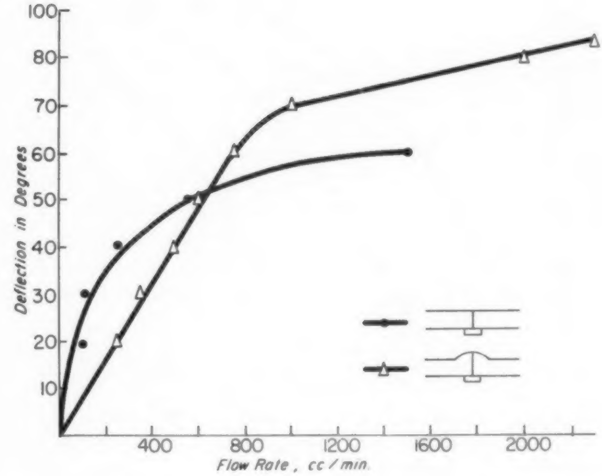

Fig. 2.—The effect of flow rate upon cupular deflection. Two forms of cupular housing were used as shown in the insert.

slightly above 60° deflection. In the case of the dome-shaped ampulla, the relation remained linear for a much wider range. There was a rather sudden departure from linearity occurring at about 65°. At higher flow rates the two curves roughly paralleled each other. The difference between the nonlinear and linear functions in the above cases is easily explained. As long as the seal of the cupula against the outer wall does not change, no matter how good or bad it might be, cupular deflection is a linear function of the flow rate. As soon as the seal is broken the relation becomes nonlinear much in the same manner as it is in the case of the straight tube. Our ampullar model happened to be constructed in such a way that a maximal cupular deflection of 68° to either side would occur within the dome. With larger deflections the cupula would leave the dome so that the seal was suddenly broken. Sixty-eight degrees, therefore, present the cut-off point of the cupula in our model.

Next was assessed what might be called Ohm's law of the semicircular canal. The flow rate was found to depend on the driving force (given by the manometer in parallel with the pump) and to be inversely related to the flow resistance within the circuit. Thereby it was unessential at which location the resistance was changed, i.e.,

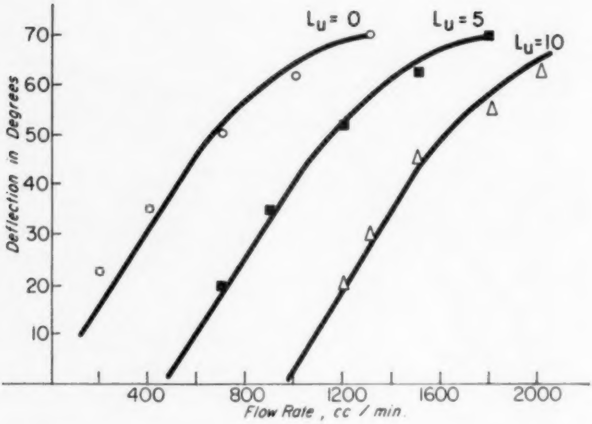

Fig. 3.—The effect of flow rate upon cupular deflection with the utricular fluid level (Lμ) as parameter.

in the small or in the ampullated crus of the canal. All that mattered was the total resistance. This indicates that the driving force might be located anywhere within the circuit. It may even be distributed uniformly over the entire circuit (as is the case in an actual semicircular canal) instead of being lumped together at one point (as is the case in our model). For constant flow resistance, then, the cupular deflection depended solely on the driving force. All this is easily understood from consideration of an analogous electrical circuit, such as that shown in Figure 1b.

However, there was one finding in this respect which needs further discussion. When the tank representing the utricle was made rather large, the relation between driving force and flow rate (and subsequently cupular deflection) became markedly nonlinear, at least at higher flow rates. The efficiency of the driving force was lessened. It was observed in such cases that the motion of fluid through the tank which was always laminary at lower flow rates, developed into eddying flow. No exact measurements were taken, but spot-checking indicated that the onset of the variation in flow resistance was in fair agreement with the change in the Reynolds number caused by the increased flow rate in a system in which the channel diameter suddenly changed from the narrow canal to the wider utricle. It is hard to predict whether or not this phenomenon of eddying is of signifi-

cance in actual semi-circular canals. The high viscosity of the endolymph may prevent the onset of utricular eddying at flow rates incurred within physiological limits.

However, if the input-output function of the peripheral vestibular mechanism would alter because of the onset of utricular eddying at higher stimulation, while that of the proprioceptive receptors would not do so, conflicting stimuli arising from these two systems would lead to an equilibrial disturbance, viz., to vertigo. This latter concept has been introduced by Malcolm. It is commonly assumed that the equilibrial triad, i.e., the vestibular, proprioceptive, and visual receptors, can work properly only when signals received by all three of them agree as to magnitude and direction. The vestibular organs, because of their lack of direct cortical representation, are thought to be receptors of a reflex system rather than true sense organs. Typical of such systems, according to Wiener, is their rigid pattern response and their inability to adapt quickly to any alteration in the stimulus pattern.

The flow resistance of our models was changed by another form of interference. This was brought about by raising the fluid level in the utricular tank above the canal's inlet and outlet, in other words, by producing intra-utricular pressure. The results of these experiments are shown in Figure 3, in which flow pressure (as read from the manometer in parallel with the pump) is plotted against cupular deflection with the utricular water level as parameter. As is seen from the shift of the entire curve with rising intra-utricular pressure, the efficiency of the driving force with respect to cupular deflection was again lessened.

This latter finding permits some speculation as to the cause of the vertigenous attacks associated with endolymphatic hydrops. If the endolymphatic fluid pressure suddenly rises in one ear an imbalance of the bilateral vestibular function may occur: due to the increased flow resistance the cupular reaction will be less in the affected than in the non-affected ear. (There will probably be no time for adaptation to this change in the receptor function before the attack subsides, in line with Wiener's concept of pattern response mentioned earlier.) The hypothesis of an intra-utricular pressure effect is supported by the clinical experience that the nystagmus is usually directed away from the affected ear, i.e., toward the more sensitive side, if one has occasion to observe it during the attack. One of the present writers (J.T.) reported recently on a hydromechanical explanation of the auditory phenomena incurred in early labyrinthine

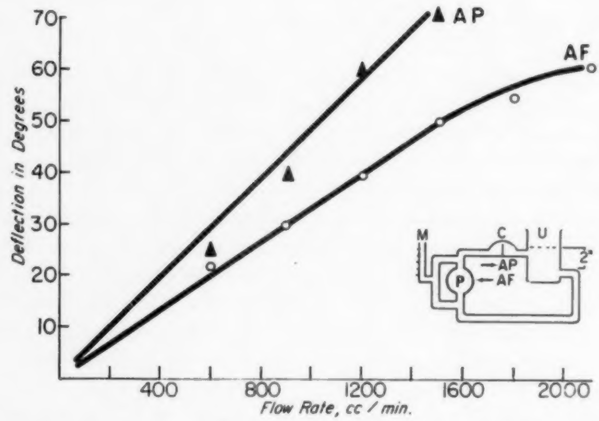

Fig. 4.—The effect of flow rate upon cupular deflection for ampullo-petal (AP) and ampullo-fugal (AF) flow directions. The utricular gravity load in this particular example was represented by a difference in elevation between the two crura of the canal of 2".

hydrops: low-tone loss, diplacusis, and harmonic distortion. Needless to say, the assumption of such vestibular and cochlear hydromechanical effects does not preclude the occurrence later on of pressure-induced degeneration of sensory epithelia as the attacks are repeated or the hydropic state is prolonged.

The last experiment in our series concerned the effect of flow direction upon cupular deflection. As long as the semicircular canal was located in a horizontal plane and the utricular inlet and outlet were at the same level, there was no difference in the effects of ampullo-petal or ampullo-fugal flow. Again in this respect the location of the driving force did not matter. It was unessential for the resulting cupular deflection whether the flow resistance of the ampullated crus was much larger than that of the small crus of the canal or vice versa, as long as the total flow resistance was kept constant. If, however, one crus of the canal was elevated above the other so that the utricular inlet and outlet were located at different heights, a gravity effect became noticeable. The weight of the utricular fluid column between the two openings of the canal aided the flow when it was directed downward through the utricle and impeded the flow when it was of opposite direction. In other words the canal now possessed what might be termed an utricular gravity load. In

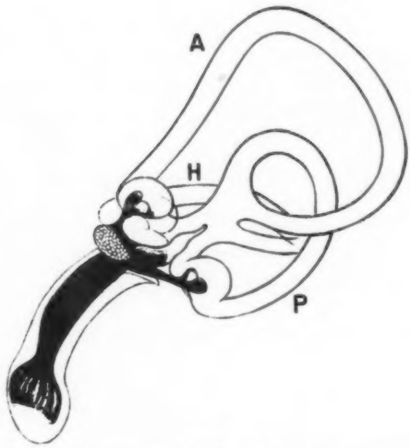

Fig. 5.—The membranous labyrinth of the pigeon from a medial aspect. A: anterior; P: posterior; and H: horizontal canals. (The lagena extends to the left, below the VIII nerve.) The organ is shown approximately in the position it occupies when the animal carries its head upright. (Adopted from Ewald; after Retzius).

the case of Figure 4 the ampullo-petal flow was aided and the ampullo-fugal flow was impeded. The difference between the effects of the two flow directions increased in direct proportion to the elevation of one canal opening over the other (not shown in Figure 4). The reason for the existence of this effect lies in the unequal distribution of mass in the semicircular canal—utricular system. If the diameters of the utricle and of the canal were equal, there could be no utricular gravity load. Likewise, the load effect would remain obscured if the acceleration caused by the force of gravity was much smaller than that incurred in stimulation of the semicircular canals. For the sake of this comparison, angular acceleration must be expressed as arc/sec^2 instead of the conventional degrees/sec^2. An angular acceleration of 360°/sec^2 corresponds to 28 cm/sec^2 (of arc/sec^2), when the axis of rotation is placed through the center of the head and the distance between the two labyrinth is assumed to be 9 cm. This is a relatively high value of angular acceleration and yet it is only a fraction of the value of gravitational acceleration (981 cm/sec^2). Therefore, the possibility is given that the utricular gravity load is a real physiological entity.

The utricular gravity hypothesis suggests a possible re-evaluation of Ewald's 2nd and 3rd laws which state: (2nd law) The effect of

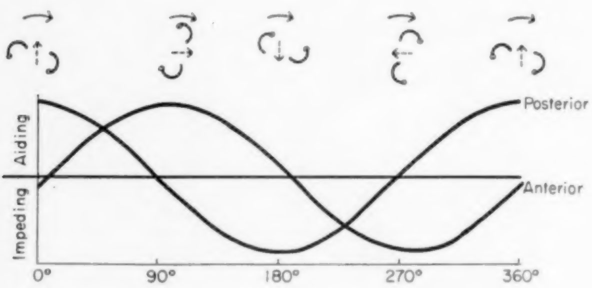

Fig. 6.—Hypothetical effect of the utricular gravity load upon contralateral anterior and posterior canals. This load is affected by a rotation through 360° within the vertical plane. The axis of rotation is arranged so that both canals are in their optimal position. The successive positions of the canals are shown on the top (i.e., left anterior and right posterior); rotation to the right (direction of arrows). The cyclic fluctuations of the utricular gravity load in both canals are shown in the lower portion. Note the phase lag between the effects upon the two canals.

ampullo-petal flow in the horizontal canal is stronger than that of ampullo-fugal flow; and (3rd law) the effect of ampullo-fugal flow in the two vertical canals is stronger than that of ampullo-petal flow. (The so-called laws of Ewald as they are quoted today were never postulated by Ewald himself as far as these writers were able to assert. In his monograph, Ewald gave a meticulous account only on 85 different vestibular experiments, most of them conducted on pigeons and ingeniously conceived and executed. Who then was responsible for the extraction of the three laws from Ewald's experimental data is not known to us.)

These two laws have been subject to adverse criticism as contradictory evidence had been accumulated by many observers. At this point, it may be well to recall Ewald's experiments Nr. 81 and 82 upon which these laws have been based. Investigating one canal at a time, Ewald had sealed it off somewhere along its curvature. Application of pressure and its subsequent release upon a small exposed portion of the membranous canal by means of a small pneumatic hammer produced brief movements of endolymph either in ampullo-petal or ampullo-fugal directions. During such tests, the animal was standing freely under a wire cage and the head movements resultant from each stimulus were observed.

Figure 5 taken from Ewald's book shows the membranous labyrinth from a medial aspect. The position is approximately that with the animal holding its head upright as was the case in Ewald's experiments (cf. Ewald's Figure 66). It is apparent from the relation of small and ampullated ends of each canal in Figure 5 that an ampullopetal flow within the horizontal canal would be gravity-aided, according to the utricular-gravity hypothesis, whereas an ampullo-fugal flow in the same canal would be gravity-impeded; also that the reverse situation exists for both vertical canals. The resultant preponderance of flow directions is in complete accord with Ewald's 2nd and 3rd laws. However, this preponderance would shift with alterations in the position of the head in relation to the gravitational axis. Therefore it would appear that Ewald's two laws cannot be applied generally but are correct for one special case only, namely, the upright position of the head.

The utricular gravity load is eliminated in the conventional turning chair test by placing the canals under test in their optimal position, i.e., in the horizontal plane. If, however, a person is rotated, with the aid of a turning wheel, in a vertical plane with the anterior vertical canal on one side and the posterior vertical canal on the other side in their optimal positions, the gravity load is not eliminated in these two contralateral canals. Such rotations are known to create an extremely unpleasant experience for the subject, sharply contrasted to that during rotations within the horizontal plane with any pair of canals in their optimal position.

An attempt is made in the following to account for this contrast in sensation. During rotations within a vertical plane, the utricular gravity load upon the two contralateral canals in question is not uniform but alters continually depending upon the instantaneous position of both crura of each canal with reference to the gravitational axis. Figure 6 shows this alteration of the utricular gravity load during one complete rotation in a schematical manner. It is apparent that there is a cyclic fluctuation of the load effect and also that there is a phase difference between both canals of slightly more than 90° with regard to this effect. Therefore conflicting stimuli are derived from these two canals leading to the manifestation of vertigo.

The utricular gravity effect might also apply to another problem, the mechanism of motion sickness. The dominant role of the vestibular apparatus in the elicitation of motion sickness has been demonstrated by Sjoeberg[6] in 1931: dogs previously susceptible to motion sickness became completely resistant after bilateral labyrinthectomy.

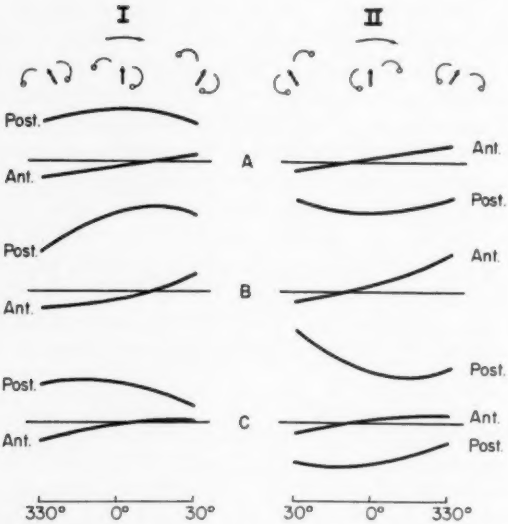

Fig. 7.—Hypothetical effect of head swaying in the plane of contralateral anterior and posterior canals. Column I: left anterior and right posterior canals with movement from left to right (direction of the arrow). Column II: left posterior and right anterior canals with movement from left to right (direction of arrow). The successive positions of the canals are given in the top row. Row A: variation of the utricular gravity load during these movements (aiding and impeding as in Figure 6); Row B: same with the g-force increasing linearily to twice its original value over the course of the movement; Row C: same with the g-force decreasing linearily to one-half of its original value over the course of the movement. (Alteration of the g-force from left to right in both cases). The angle described by the movement has been made rather large (30° from the midline to either side) for the sake of better illustration.

One of the present authors has duplicated this study and confirmed Sjoeberg's results (J.T. unpublished data; 1952).

A special form of motion sickness, the elevator sickness, presents the problem in an abstract form, since motion is confined to both vertical directions. Elevators have provided adequate stimulation in laboratory experiments in motion sickness (Wendt). Johnson et al[2] noticed that the onset of elevator sickness in their subjects was always accompanied by swaying head motions and they were subsequently[3] able to reduce the incidence markedly by fixing the head of susceptible persons in a plaster cast.

It may again be the action within contralateral anterior and posterior canals which provides an explanation. These canals are affected by swaying head motions (each pair of such canals, optimally, by tilting the head slightly forward and sideways or backward and toward the opposite side). Two examples of such motion are shown schematically in Figure 7. The first set of curves (A) represents the pattern of the gravity load during this particular movement under the condition of a steady g-force. The fact that the gravity load upon the two canals is of opposite sign for the greater portion of such movements has obviously no effect by itself. The arc described is rather small (in reality it may be much smaller than that assumed in the drawing). If, however, the g-force increases (Fig. 7., B) or decreases (Fig. 7., C) at the same time when such movements are executed, the load pattern is drastically altered. This again presents a case of conflicting stimulation and if repeated a sufficient number of times may well lead to motion sickness.

Fig. 8.—Two forms of cupular housing.

CONCLUSIONS

The results presented here concern very elementary principles of hydromechanics in closed circuits which bear some resemblance to the utriculosemicircular canal system. An attempt was made to develop a working concept of vestibular hydromechanics. No real proof has been offered as to the mode of reaction of the actual organs; rather, new avenues of investigation have been suggested which are hoped to yield more definite solutions after these working principles have been applied to animal research. The attempt at using these tentative results for the explanation of some well known vestibular phenomena is hypothetical at best. The authors hope that they have left no doubt as to where the description of facts left off and where speculation began.

APPENDIX

The difference between the two functions of Figure 2 concerning current flow vs. angle of deflection can be expressed by simple math-

ematical considerations. Figure 8 shows again the two forms of cupular housing used.

The symbols of these drawings and those used in the following computation have the following connotation:

i - current flow	v - length of flap
p - pressure upon cupular flap	α - surface area of flap
R - flow resistance of flap	σ - gap on top of flap

Θ - angle of deflection

According to Ohm's law, we may write

$$p = i\ R. \tag{1}$$

We may also state that the angle of deflection depends upon the pressure exerted upon the cupular flap:

$$\Theta = \text{constant}\ p. \tag{2}$$

(The constant of equ. (2) is determined by the surface area of the flap, viscosity, and other factors). From (1) and (2) follows

$$\Theta = \text{constant}\ i\ R. \tag{3}$$

The flow resistance of the flap is proportional to its own area and inversely related to the size of the gap through which fluid may escape. Consequently,

$$R = \frac{\alpha}{\sigma} \tag{4}$$

Within the dome-shaped ampule, the size of the gap remains constant as long as the flap stays within the dome. Therefore, the entire term (4) is constant. Substituting (4) in (3) and lumping all constant together into a single one (k) yields

$$\Theta = k\ i. \tag{5}$$

That is, the deflection of the flap is proportional to the current flow as long as the size of the gap does not alter. That was precisely what the curve b in Figure 2 had shown.

In the case of the straight cupular housing, however, the size of the gap alters with the angle of deflection. As seen from Figure 8 b, the increment of the gap is given by the difference between the

length of the flap minus the distance BC. The latter forms one side of the right triangle ABC of which one angle and the hypothenuse are known. Consequently

$$BC = v \cos \Theta. \tag{6}$$

The increment of the gap is then given as

$$\sigma^1 = v - v \cos \Theta = v\ (1 - \cos \Theta). \tag{7}$$

Since the original size of the gap was presumed to be small, we may neglect it in the following and take the increment for the size of the gap at each angle of deflection. If the size of the gap varies with the angle of deflection, the flow resistance is not constant either. By substituting term (7) in equ. (4) we obtain

$$R = \frac{\alpha}{v\ (1 - \cos \Theta).} \tag{8}$$

Finally, substituting (8) in (3) and again lumping all constants together in one single term (k^1) yields

$$i = k^1\ \Theta\ (1 - \cos \Theta). \tag{9}$$

Inserting numerical values in equation (9) produces a curve which is identical to curve a in Figure 2.

University Hospital
Bell Telephone Laboratories, Murray Hill, N. J.

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XLIX

AN EXPERIMENTAL STUDY OF AUDITORY THRESHOLD ACUITY IN CHILDREN WITH CEREBRAL PALSY BY PGSR AND OTHER TECHNIQUES

IRWIN LEHRHOFF, PH.D.

BEVERLY HILLS, CALIF.

Although galvanic skin response has been known since 1879, when Vigouroux[1] first called special attention to the variations and variability of the electrical resistance of the human body, Féré's[2] work in 1888 paved the way for the recording of electrical phenomena from the skin. However, more recently, Bordley and Hardy[3] have pioneered in adapting this response to audiometric testing. Because of their work, considerable interest has been aroused in the use of psychogalvanic skin resistance audiometry in testing the hearing of infants and young children.

The study and validity of PGSR audiometry with normal hearing children was one of the purposes of this study. However, the major purpose was the evaluation of PGSR audiometry with cerebral palsied children. Testing auditory threshold acuity of cerebral palsied children is often a difficult task. Obstacles such as involuntary movement, unintelligible speech, frequent mental involvement, questionable comprehension, and the unreliability of testing methods with the cerebral palsied all hinder the experiment. Differential diagnosis often involves a choice between hearing loss, delayed speech because of the physical involvement, mental retardation, emotional withdrawal, and aphasia. Indecision regarding the child's hearing capacity may also hinder rehabilitation. There is a need for a clinically objective hearing evaluation of the cerebral palsied population, especially for those children who cannot respond to conventional pure tone or speech audiometry.

The experiment was set up so that auditory thresholds of the cerebral palsy and control groups could be compared by pure tone and PGSR audiometry. Experimental design was directed by the following questions:

1. Is there any relationship between auditory thresholds in normally hearing childen and in normally hearing cerebral palsied children secured by two methods: a) pure tone (air conduction), b) galvanic skin response?

2. Does the galvanic skin response yield valid and reliable results with cerebral palsied children?

3. How do the latent periods of the galvanic skin response compare in the normal and cerebral palsy groups?

4. Is any relationship apparent between frequencies for either the normal or cerebral palsy groups?

5. Is any relationship apparent between right and left ear?

6. Do the audiometric data reveal any statistical differences between spastic and athetoid groups?

SUBJECTS

Thirty normal subjects and 60 cerebral palsy subjects, all male children, served as the source of data for this study. All of the subjects, the cerebral palsied and the control group, had normal hearing. The basic criteria for normal hearing included: 1) no abnormal findings after a complete otological examination; and 2) no more than a ten db loss for any two successive frequencies in either ear on the basis of a pure tone air conduction audiometer test.

Controls. Forty-two normal male subjects were screened for possible use in these experiments, and of this group thirty were selected as subjects. The age range was from seven to twelve with a mean of 9.1. The subjects were school children from various elementary schools. Classification of the individual as a normal child was made on the basis of five criteria: 1) no abnormal findings after a complete medical examination given within three months of the onset of testing; 2) a parent interview in which no concern was manifested about the child's normality; 3) no history of any known physical or mental defect; 4) a school interview with the classroom teacher which showed perfectly normal behavior in the classroom; and 5) no evidence of any deviation from average behavior which was noted in a conversational period conducted prior to the experiment.

Cerebral Palsy. Two groups of cerebral palsy classification, athetoid and spastic, were set up and 30 subjects were chosen for each group. All subjects were patients of the State Cerebral Palsy Diagnostic and Treatment Clinic at the Children's Hospital Outpatient Department, Los Angeles, Calif.

Diagnosis and classification of cerebral palsy was made on the basis of three criteria: 1) referral of the child to the hospital from the State of California Department of Public Health Bureau of Crippled Children's Services with a medical diagnosis of cerebral palsy; 2) diagnostic examination by the medical director of the cerebral palsy program at Children's Hospital; and 3) consultation reports of a staff conference composed of a pediatrician, an orthopedist, and a neurologist.

The age limits of the two groups were: 1) spastic — seven through twelve years with a mean of 8.4; and 2) athetoid — seven through twelve years with a mean of 9.7.

Selection of Cerebral Palsy Subjects. The subjects were selected after careful screening of 1,226 file cards and 320 charts of cerebral palsy children under the state cerebral palsy program. The first step was to screen the I.B.M. file cards and set aside those who were within the desired age group, diagnostic classification, and average intellectual range. Three hundred and twenty children fell within these classifications. Their medical charts were carefully reviewed until the 60 ultimate subjects were selected, 30 spastic and 30 athetoid. Variable factors were taken into account, and controlled as much as possible. Each child selected had an electroencephalographic test and psychometric workup. These were equated with schooling. These children were also seen by the experimenter on their clinic vists over a two-year span which facilitated rapport, so necessary for testing hearing of children.

EQUIPMENT

1. An Experimental Maico Psychometer, Model WD 10084. The Maico electrodes and shocking device were not used. There appeared to be too much adaptation to the Maico shock and the electrodes proved to be unwieldy and did not present a good surface of contact which would have introduced a large variable. Other described components were used.

2. A shock apparatus utilizing a condenser discharge circuit.

3. An ADC audiometer with binaural headphones.

4. A Wallace and Tiernan, Model F-194, 0-5 milliampere D.C. ink recorder, with recording graph. A circular recording type graph was used, which made it easier to read the entire report and facilitated the length of recording possible.

The psychometer was connected to the Wallace and Tiernan D.C. Recorder which is a moving magnet type instrument adapted to record small changes in electric current. It provides a range from zero to five milliamperes. The operation is provided by a circular alnico magnet. A small 115 volt A.C. motor and cam provide a slight tapping effect which tends to overcome bearing friction and pen drag and causes the magnet and pen assembly to assume its correct position, and reach it with a minimum of delay. The chart drive is powered by another 115 volt A.C. synchronous motor, which turns the dial four revolutions per hour.

PROCEDURE

PGSR testing was administered first, because it was felt that this would be a more objective procedure: first getting a GSR graph and then matching it with pure tone tests. All testing was done at the University of Southern California Speech and Hearing Clinic in a sound-treated and control room in the audiological suite. The subjects were seated comfortably in a large armchair with one parent seated near them for reassurance. The parent was asked to avoid direct contact, even eye contact with the child. The examiner and equipment were in the adjoining control room. The earphones and wires leading from the electrodes were all that were visible to the subject. The child was placed where all of his movements and actions could be easily observed. Since rapport had previously been established, and these children were in a high age range, no toys were introduced and distractions were kept at a minimum. Each subject was briefly informed about the nature of the testing and reassured about the procedure, although no mention was made about the stimuli involved. To reduce the recording of muscle movement artifacts, especially in the cerebral palsied group, each subject was informed of the effect on the record of any such movement and was instructed to relax and remain quiet. Co-operation was good and muscle movement was minimal. At times, a few rest periods were needed, and then testing was resumed. It was felt that the environment of the test situation was controlled, array of distracting stimuli reduced, and the child's behavior stabilized so that responses significant of hearing were interpretable. A hearing response was char-

acterized by two definite breaks on the graphic record with the deflection of the pen moving toward the periphery of the graph.

The electrodes used in the experiment were made from circular zinc discs three-fourths of an inch in diameter soldered to twelve-foot leads connected to an Amphenol plug and plugged into the psychometer and shock device. Two pairs of electrodes were used, one for pickup and the other for shock. Each pair of zinc discs were fastened to a two-inch wide rubber band by soldered screws. The electrodes were coated with a paste made of kaolin in a saturated solution of zinc sulphate before being placed on the subject. The shock electrodes were attached to the rubber band one inch apart and the band was then fastened to the left leg of the subject, being held in place by either scotch or adhesive tape.

The pickup electrodes were attached to the rubber band four inches apart so that when the band was wrapped around the left hand the electrodes were fastened to the palmar and dorsal sides. The graph was started and the child's basic wave pattern observed for a few minutes while the line of base resistance was set. The base line was set at the periphery of the circular graph and the pen was deflected toward the outside. Then binaural earphones were placed on the subject.

The child was conditioned, using a 1000 cps tone at 30 db with reference to audiometric zero as the initial conditioning tone. A few intermittent shocks were given at various other frequencies throughout the testing as a reinforcement to offset adaptation and variable attention. A 1000 cps tone was used for conditioning, since these were normal ears.

A shock apparatus utilizing a condenser discharge circuit gave better conditioning results than a Harvard Inductorium faradic shock in a preliminary pilot study and was, therefore, used in this study. The condenser discharge circuit produced shock that showed less pain and less annoyance than the faradic shock and still maintained the necessary conditioning. A higher intensity of shocking could be used without producing as much traumatic effect.

The tone was given and then followed in four seconds by a shock. The shock was first administered at a sub-liminal intensity which is estimated at 15 millivolts and was gradually increased as was necessary for each individual subject. Conditioning was established when galvanic responses occurred for tone alone. Some sub-

jects did not need any shock for conditioning; galvanic responses were registered for tone alone, but on the average three to five pairs (tone followed by shock) were necessary for satisfactory conditioning.

Standard audiometric technique was used for the testing of both ears with responses indicated by definite wave forms on the recording apparatus. The latent period from the time of the presentation of the shock and tone to the beginning of the galvanic response was recorded on the graph by electronic timers. The child was closely watched through the observation window for all movements that would affect the graph, and these were noted. The graph was then charted and transposed to a regular audiogram.

Within seven days of the completion of the PGSR test, the child returned to the clinic, and a pure tone test was administered in the standard manner.

RESULTS

The experimental data consisted of seven threshold determinations for each ear from ninety subjects resulting in 1,260 responses for each of two pure tone testing techniques.

An analysis of variance was computed on these data with the results being divided into classifications of four sources of variance: 1) frequency; 2) methods of testing threshold acuity; 3) ears; 4) groups.

For brevity, pure tone will stand for conventional pure tone audiometry as differentiated from PGSR. Both tests employ pure tones delivered by air conduction to the ear, but the method of responses employed is different.

Data were computed for each of seven frequencies. There was very little difference between the frequencies.

Interactions of frequency with either methods of testing, groups, or ears, were not significant.

Auditory threshold acuity for each frequency was tested by PGSR and subjective pure tone air conduction methods, and a comparison was made between the standard pure tone and PGSR audiometry.

The db difference between the two methods ranged from 3.65 db to 4.32 db with a mean difference of 3.94 db for all groups.

Only the pure tone threshold of 4096 cps had a positive mean of 0.18. All other thresholds showed better auditory acuity than the calibrated zero of the audiometer. When these threshold means were broken down into specific groups, the average mean difference between PGSR and pure tone results for the normals was 4.00 db, 2.73 for the spastics, and 5.07 db for the athetoids. Thus the mean difference for all groups between the two methods showed a very close relationship. However, the responses for individual subjects on pure tone audiometry remained very close to the mean, while PGSR responses were more widely scattered from the mean, especially in the cerebral palsy groups. The galvanic skin response was variable because skin reactivity is a variable and often unstable phenomenon. Constant vigilance was needed to exclude extraneous stimuli which might have altered the graph. Involuntary movement of the cerebral palsy group had to be carefully watched so that movement which produced artifact deflections on the graph were not interpreted as hearing responses. The technique proved difficult in application with the severely involved cerebral palsied and the margins of significance in electrical change were often narrow.

The magnitude of the response appeared to have a positive relationship to the intensity of the stimulus. The deflection of the pen for a stimulus tone 30 db above threshold was greater than for tones closer to threshold. But this did not hold true at all times and no attempt was made to measure this relationship.

The rate of recovery of the GSR following the reaction to the stimulus showed an inverse relationship to the initial resistance level of the subject. When the initial resistance was moderately high (60,000 ohms) the recovery of the galvanic skin response following the peak of reaction was very slight, but when the resistance level was much lower (20,000 ohms) the recovery was much more marked. This agrees with the studies of Darrow[4] on the relation of the GSR recovery curve to resistance levels.

GSR thresholds approximated pure tone thresholds within 5 db for the normal children with normal hearing, and their results closely bunched around the mean. This same comparison with the cerebral palsied was much more unstable.

The data derived from each ear separately were treated separately, so that inter-ear comparisons might be made. Although thresholds

of the two ears were derived separately, the degree of correlation between the two was very close.

There was very little difference between the ears at any of the frequencies. These results showed that the groups responded differentially to method, but not as to right or left ears. Differences between ears remain as chance variation. This supports the thesis that these were normal ears.

No galvanic skin responses could be obtained from 14 spastic and 18 athetoid subjects, so that their pure tone and PGSR results were not entered in the comparison.

The differences between the groups were not only statistically significant, but also clinically significant. The pure tone air conduction data between the groups corresponded very closely with each other and with the National Health Survey[5] of 2,484 tested ears. Pure tone data grouped around the defined audiometric zero, but this was expected since these were all normal hearing children.

However, PGSR results between the normal control group and the cerebral palsy groups were statistically and clinically different. The galvanic skin response on the graph was so different for the brain damaged group that the experimenter could sort the control and cerebral palsy graphs without knowing the differential diagnosis. Five specific differences in the GSR for the cerebral palsy groups were noted:

1. *Latent Period.* The latent period from the onset of stimulus to the beginning of the reaction was longer and more variable for the cerebral palsied. Latent period comparisons for all groups are shown in Table I.

The normal group ranged from 1.70 to 2.05 seconds with an average mean of 1.80 seconds. The range for spastics was much higher from 5.50 to 6.70 seconds and 5.84 second average. The range for athetoids was still higher, from 5.75 to 6.90 seconds, and their average was 6.35 seconds. While only .51 seconds separate the two cerebral palsy groups, the difference between the normals and the lowest cerebral palsy average was 4.04 seconds. Latent period differences correlated against frequency were not significant.

Latent periods for the normal group were always within 1.5 to 2.5 seconds but the cerebral palsy latent periods ranged from a few seconds all the way to 38 seconds on one subject.

TABLE I

PGSR MEAN THRESHOLD LATENT PERIODS FOR THE THREE GROUPS PRESENTED IN SECONDS

FREQUENCY	NORMALS	SPASTICS	ATHETOID
128	1.70	5.95	6.15
256	1.70	5.60	6.75
512	2.05	6.70	6.50
1024	1.95	5.50	6.05
2048	1.70	5.50	5.75
4096	1.75	5.50	6.90
8192	1.80	6.10	6.30
Total	1.80	5.84	6.35

2. *Conditioning.* The cerebral palsy group needed more initial shocking to set up conditioning and even after the conditioned reflex was obtained, more reinforcement was needed than for the normal children. A conditioned response could not be obtained on some of the cerebral palsy subjects, even though as many as eight to twelve shocks were given these children. These children stated that they felt the shocks and there was a noticeable jumping reaction each time the shock was administered, but there was no galvanic skin response recorded on the graph. There was no conditioning difficulty with the normal group. A conditioned reflex was obtained for every subject.

3. *Skin Resistance.* Skin resistance for the cerebral palsied was typically low. Hardy and Pauls[6] state that in a room temperature of approximately 70° F., normal skin resistance for children ranges between 50,000 and 120,000 ohms, but during very hot weather, skin resistance may be as low as 5,000 to 25,000 ohms. These statements coincided with results for the normal group, but resistance for the cerebral palsied was continuously low.

4. *Description of the Response.* Five differences were noted in the response itself between the cerebral palsy and normal groups. Within the realm of this experiment, no satisfactory interpretation can be made.

a) Base Line. The base line for the normal group was consistent throughout the test. However, the base line for the cerebral

palsy group showed a constant drifting, usually in a direction toward the center of the graph.

b) Peaks. The peaks of the cerebral palsied response were sharper, more pointed, and of a shorter duration. The normal subject's response was usually characterized by two breaks on the graphic record, while the cerebral palsied exhibited a crescendo type of response.

c) Activity of the Response. The cerebral palsy graph showed continuous short bursts of activity. The pen of the recorder would move along in a slow inactive pattern and then, suddenly, a hyperactive volley effect would occur without any apparent reason. Then after a few minutes, the pattern would again resume its slow inactive stage. The GSR pattern for the normal children remained consistent for each individual throughout the test.

d) Recovery Interval. The rate of recovery of the GSR for all groups following the reaction to the stimulus showed an inverse relationship to the resistance level of the subject. However, the cerebral palsy group exhibited a slow, steady drop from the peak of the response rather than the rapid short drop which was characteristic of normals.

e) Reversal of Polarity. Only in the cerebral palsy group was the reversal of polarity phenomenon seen. The deflection of the pen for the galvanic skin response moved toward the periphery of the circular graph for the normal children. In the cerebral palsy groups, the pen might start out deflecting towards the periphery, but at various times, would shift and deflections would record toward the center of the graph. This reversal might remain for a few minutes of responses, and the deflections of the pen would shift back toward the graph's periphery again. When these polarity reversals occurred, the latent period, description of the response, and recovery interval were similar to the response occurring in the other direction. This reversal of polarity was not found by Hardy in his cerebral palsied children, according to a personal communication, so that this phenomenon may actually be an artifact of the equipment. However, it did not occur with the normal children.

5. The GSR could not be established for 14 spastic and 18 athetoid subjects. No difficulty was encountered in obtaining pure tone data, but the GSR could not be elicited. The response was absent in 46.7 per cent of the spastics and 60 per cent of the athetoids tested.

Half of these did not respond to shock alone; the remainder showed a large response to shock, but no reflex could be established to tone alone. The question presents itself as to why some of the brain-damaged children give good responses and others no response at all. And why does this absence of response not occur with normal children? The possibility that the galvanic skin response is at least in part cortically controlled needs to be studied.

A comparison of mean differences between the spastic and athetoid groups does not demonstrate any conclusive evidence for differentiating the two groups. However, the cerebral palsy and normal groups differed statistically and clinically.

CONCLUSIONS

There was close relationship between auditory thresholds of normal hearing children and normal hearing cerebral palsy children secured by methods of PGSR, and by pure tone audiometry. PGSR threshold means were four decibels below those obtained by pure tone air conduction methods.

The galvanic skin response did not yield valid and reliable results with cerebral palsied children in this study. It was felt that the GSR is at least in part cortically controlled. The GSR graph was radically different from that of the normal. Latent periods of the galvanic skin response differed significantly at the one per cent level for the normal and cerebral palsy groups.

Differences between frequencies for the normal and cerebral palsy groups were only chance variations.

Differences between right and left ears for either the normal or cerebral palsy groups were not significant.

Differences of audiometric data between spastic and athetoid groups were not significant.

PGSR audiometry introduces an objective element into testing of auditory threshold acuity of cerebral palsied children but does not dispose of all the problems. It should be used as an aid to other testing procedures, case history, and observation, and not as an ultimate end. PGSR testing should be used with caution with all cerebral palsy children until further research is completed on such

critical points as technique, artifacts, placement of electrodes, and the mechanism of the galvanic skin response itself.

436 North Roxbury Drive

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Scientific Papers of the American Laryngological Association

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A NEW SURGICAL TECHNIQUE FOR THE VOCAL REHABILITATION OF THE LARYNGECTOMIZED PATIENT

JOHN J. CONLEY, M.D.
NEW YORK, N. Y.
FELIX DEAMESTI, M.D.
(By Invitation)
SANTIAGO, CHILE
MAX K. PIERCE, M.D.
(By Invitation)
LOS ANGELES, CAL.

One of the most distressing aspects of the total laryngectomy operation is the loss of the ability to produce sound. The threat of the denial of this projectory capacity causes the patient confusion and depression. In his efforts to avoid this unhappy situation he has often delayed or even substituted an inferior method of treatment for his disease, and in some instances forfeited his life.

It is true that there are rehabilitative measures available in the use of the esophageal voice or mechanical appliances. The latter are cumbersome, and their substitution for the human voice is so inferior that few patients accept them. Technical improvements in these mechanical aids are badly needed and long overdue. The use of esophageal speech has been very effective in many instances, yet it requires considerable discipline and effort for months postoperatively, under the leadership of a vocal rehabilitationist. Some patients attain a high degree of proficiency in this method but many more are left

From the Head and Neck Department, Pack Medical Group and the Surgical Service, St. Vincent's Hospital, New York, N.Y.

with inadequate voice, and some are simply not rehabilitated. Forty per cent discontinue training against the advice of the therapist. The reasons for these failures are associated with the size and character of the wound relating to the excisional operation and the psychological determinations of the patient.

It was hoped that a new operation to supply adequate air easily for phonatory purposes would eliminate the "gulping" technique, and permit the patient to talk with ease. It is likely that this technique will prove to be more of a help in accomplishing a speech technique than a permanent part of the particular activity of speaking. It was recognized that this new voice would never attain the capacity of the natural vocal organ, yet the ease of speaking postoperatively might partially remove one of the serious disadvantages to the operation which has proved most effective against cancer of the larynx.

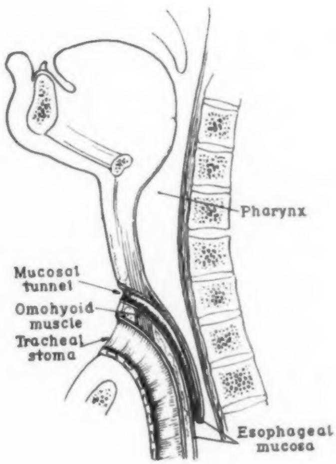
INDICATIONS

The vast majority of patients on whom vocal rehabilitation operations can be considered fall into the group where extirpation of the larynx and associated organs have been carried out for the treatment of cancer. This includes laryngectomies alone, or as part of the composite operations incorporating the lateral neck, pharynx, tongue and mandible. The new technique can be carried out at the time of the primary excision, or as a separate, secondary procedure. Individuals who have had the larynx destroyed by irradiation comprise a smaller group who can usually not be benefited by vocal rehabilitation operations.

Individuals who have been subjected to extirpation of the larynx and have not mastered esophageal speech, or adjusted to an artificial mechanism, and who desire speech development, may be considered for the rehabilitaton operation.

THE PROBLEM

The technical problem to overcome consisted of creating a passageway that would permit the free flow of air from the trachea into



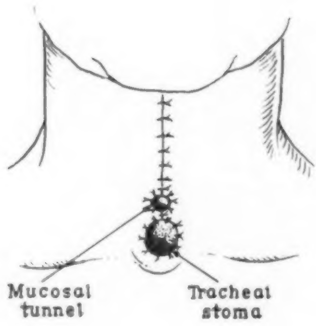


Fig. 1.—Mucosal tunnel opens just above tracheostome and extends inferiorly along esophagus.

Fig. 2.—One position for tunnel opening.

the esophagus without the passage of food or saliva from the gullet into the trachea. The great inconvenience caused by an inadvertent small pharyngeal or esophageal fistula would unquestionably condemn any such uncontrolled communication. It was therefore conceived that the communication should provide the following principles:

1. It should be tubed, as a tunnel or flap.

2. The act of swallowing should close the tunnel automatically.

3. The tracheal air inlet should be 3 to 5 cm higher than the internal esophageal opening.

4. A muscle should be used to suspend the superior portion of the tunnel.

5. The main portion of the tunnel should be positioned in the narrowed area of the esophagus so that the passage of food or fluid

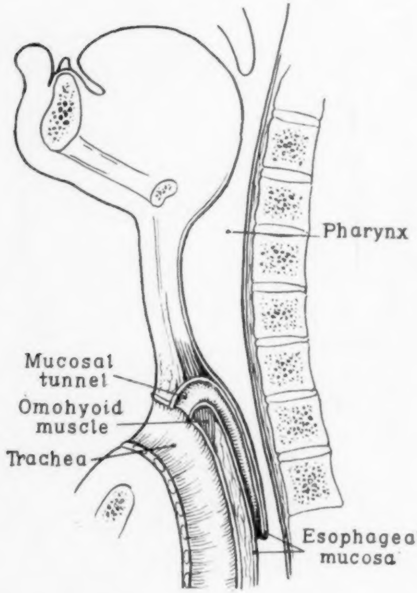


Fig. 3.—Mucosal tunnel opens in trachea, extends upward then inferiorly. It is suspended on a neck muscle (omohyoid).

through this area would enhance the collapse of the tunnel and prevent the "fistula" phenomenon.

6. The external opening should be easily adapted to the airway system so that exhaled pulmonary air could be directed into the gullet for phonatory purposes, without a complicated apparatus.

THE OPERATION

It is essential that adequate preparation for this operation be carried out in the experimental laboratory on dogs and cadavers. When the procedure is incorporated as part of the primary excisional operation of the larynx and associated tissues, a mucosal flap is created

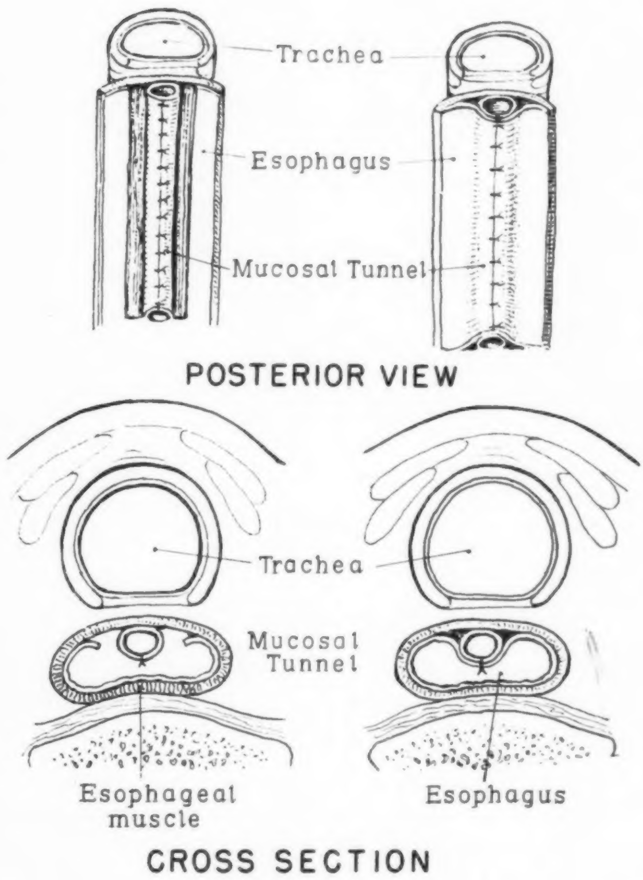


Fig. 4.—Mucosal tunnel made from esophageal lining with openings in esophagus and trachea.

along the anterior portion of the cervical esophagus. The dimensions of the flap are 1½ cm wide by 5 cm long. Its position may begin at the borders of the external wound of the cricopharyngeus or several centimeters lower in the esophagus, to accommodate the remaining musocal pattern and also the tracheostome. The muscular element of the esophagus is not included in this flap. The flap is then tubed with No. 5-0 atraumatic chromic catgut over a No. 9 rubber catheter, with the mucosa forming the inside lining of the new tube. The lateral walls of the esophagus are approximated over this tube, thus forming a mucosal tunnel emerging from the lower anterior wall of the esophagus. The catheter remains as a stent in the tunnel for six weeks. It communicates with the esophagus below and with the external portion of the neck above. This catheter is tied off so that it will not leak. The superior portion of the tunnel is then fixed to a buttonholed aperture in the posterior part of the trachea, or sutured just above the tracheostome, according to the relative positions of these structures. A muscle sling or loop may be positioned under the upper segment of the tunnel in an attempt to assist in its compression upon swallowing. The omohyoid or scalene muscles were used for this maneuver. Three cases did not have the muscle sling and worked satisfactorily. The pharyngeal and neck wounds are closed in the routine manner following laryngectomy and excision of associated tissues.

The use of an autogenous anterior jugular vein has been used upon two occasions to create the communication of the tracheal air with the esophagus. This free graft is inserted in a tunnel in the adventitia of the anterior esophageal wall 5 cm long. At the inferior aspect of the tract the vein threaded over a No. 8 catheter perforates into the lumen of the esophagus. The superior segment of the vein graft is attached at the opening of the trachea or in the skin just above it. This vein graft is not in direct contact with the mucosal pharyngeal repair but approximately 2 to 3 cm below this critical area. The technical features of the vein graft operation in this instance are much easier to carry out than the creation of the mucosal tunnel.

In individuals who have been given the opportunity to study hypopharyngeal or esophageal speech and have failed to rehabilitate their voices, and individuals who have had not only laryngectomy but unilateral or bilateral neck dissection, where normal vocal rehabilitation is considerably more difficult, a modification of the tunnel tech-

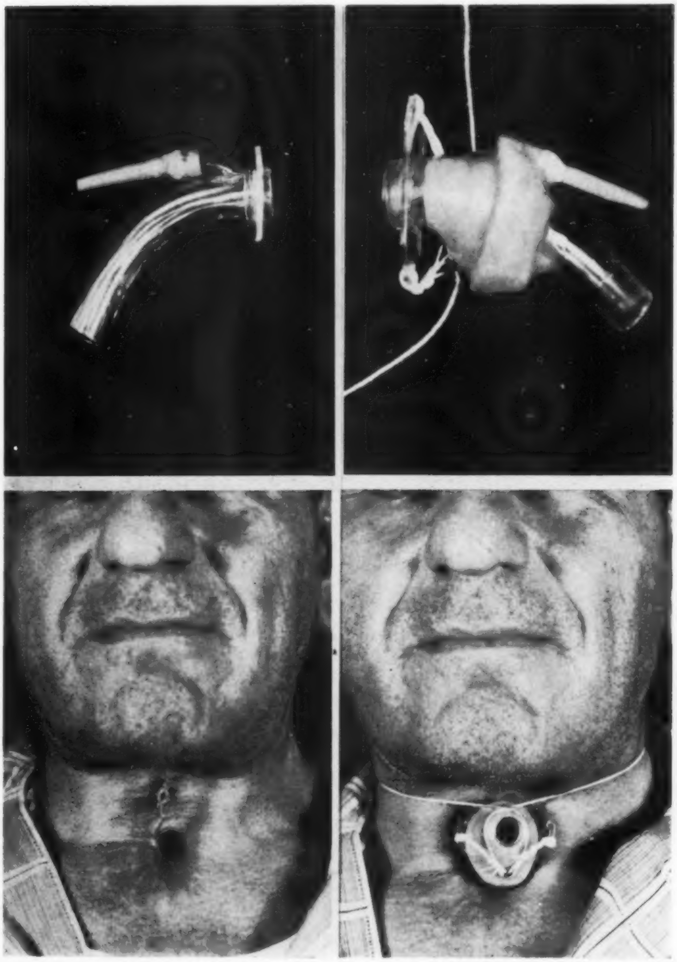


Fig. 5.—Original plastic tracheostomy tube with tunnel adapter. This adapter is custom fitted to the size and angle of the mucosal tunnel.

Fig. 6.—A. Airway Adapter. B. Patient, showing controlled tunnel. C. Patient, showing adapter in position in trachea and tunnel.

Fig. 7.—Lipiodal study of operative area showing tracheostomy and mucosal tunnel.

nique is applied. A free mucous membrane tubular graft approximately 5 cm in length is procured from the inferior buccal aspect of the oral cavity and tubed over an appropriate catheter. Full thickness supraclavicular skin has been used for the same purpose. By means of a puncture wound and stylet this free mucous membrane graft, or skin graft, is inserted into the space between the trachea and the cervical esophagus. It is threaded through this space inferiorly for a distance of approximately 5 cm. Under direct laryngoscopy it is perforated through the anterior wall of the cervical esophagus. The catheter is maintained in position for six weeks or longer if there is a tendency toward stenosis. The patient is fed with a nasogastric tube for the first four postoperative days.

After an interval of two weeks postoperatively, the patient can use the new esophageal tunnel to facilitate his speech rehabilitation. This is accomplished by the use of a specially adapted plastic tracheostomy tube with a superior connecting outlet over which a soft rubber tube can be fixed in order to fit into the new mucosal tunnel. The air stream is directed by placing the finger over the external opening of the tracheostomy tube. This might be improved by the use of a flutter valve.

RESULTS

The technique has been carried out on fifteen patients, twelve primary procedures and three delayed procedures. Of the twelve primary procedures there were three technical failures, two stenosis of the tube and one fistual formation. It is believed that the stenosis resulted from removing the catheter stent after seven to ten days, thus permitting scar to close the tunnel. This caused no added inconvenience to the patient. The patient with fistula formation had been treated with irradiation prior to his laryngectomy. The fistula leaks intermittently when the patient takes liquids by mouth, but has not caused him enough inconvenience for him to request it to be closed, as a minor office surgical procedure, for a period of over eighteen months. Two of the successful patients leaked a few drops as a result of pressure from a poorly adapted air tube connection. This improved when the curve and length of the tube was corrected. It is conceivable, however, that the delicate plastic tunnel could be destroyed by pressure and abuse from the adapter.

With simple instructions, patients can usually speak on the first effort. The quality of the voice is essentially that of pharyngeal or esophageal speech, with better air control and supply, and greater ease of production. It has assisted all in understanding esophageal speech techniques and in using the two methods in combination.

Four patients rarely use the tube now that they have become accomplished in esophageal speech through their own training. The presence of this tunnel is not an inconvenience.

CONCLUSIONS

1. A new surgical technique for the vocal improvement of the laryngectomized patient has been presented.

2. It consists of creating a mucosal tunnel through the wall of the cervical esophagus, causing a controlled communication between the trachea and gullet. The tube is constructed in such a manner that air can pass into the esophagus without the disadvantage of food and saliva passing onto the neck or into the trachea.

3. It is not a dangerous procedure and can be carried out with an acceptable margin of success.

4. There is an obvious and immediate improvement in the patient's adaptive capacity to the laryngectomized status.

5. It is hoped that this will stimulate thought in this neglected field with advancements in speech rehabilitation instruction and technical aids for these patients.

6. Results from the operative technique warrant further investigation.

139 E. 36th St.

Prosthesis made by Joseph A. Salviolo, D.D.S., New York City, N.Y.

LI

THE CHANGING YEARS: THEIR IMPACT UPON THE MANAGEMENT OF PARANASAL SINUS DISEASE

FREDERICK T. HILL, M.D.
WATERVILLE, MAINE

The changing years, particularly those of the past four decades, have been characterized by great scientific developments which have had a tremendous impact upon the practice of medicine. Our own specialty of otolaryngology not only has been broadened in scope but, along with other fields of medicine, has been provided with skills and facilities for more accurate diagnoses and more effective therapy. Nowhere may we find a better example of these changing years than in the management of paranasal sinus disease.

To one privileged to have practiced otolaryngology throughout this period, it has been interesting to observe these changes and to witness the gradual fitting into pattern of the contributions of many individuals. In attempting to review this period in its relation to the treatment of acute and chronic sinusitis I shall use as the basis for my observations the material in the Transactions of the American Laryngological Association since the year 1918. Obviously this cannot be all-inclusive, but should suffice for this purpose, it being illustrative of the contemporary thinking of this period.

One must admit being chagrined at much of the earlier therapy, some of which justified the formerly heard popular statement. "Once a sinus, always sinus." This was too often true in the pathological as well as the anatomical connotation. But, lest we be too critical, let us remember that our leaders of this earlier day lacked many of the advantages so readily available today. Perhaps their greatest asset was an excellent knowledge of the involved anatomy. Indeed it was a far cry from the days of Dr. Oliver Wendell Holmes who, in his anatomical lectures at Harvard Medical School, routinely dismissed the ethmoid with these words, "Gentlemen, today we take up the ethmoid. Gentlemen, damn the ethmoid."

But skilled as they were in anatomy the physiology of this region was little understood or appreciated. It was to be left for Proetz to lead us to a belated interest in normal function, as well as reaction to the abnormal. The autonomic nervous system, the endocrines, the body electrolytes and their possible relation to our problems had received little, if any attention. The importance of constitutional or environmental factors was scarcely recognized. Stress, as a phenomenon, had not received consideration. Chemotherapy and antibiotic therapy were yet to become available. Allergy simply meant altered reactivity and had little intelligent application. Still our predecessors labored well with the tools available to them and while so doing, worked and encouraged others to work, seeking the answers to their many problems.

Focal infection was in its heyday in the earlier part of this period and the surgical removal of almost every accessible organ in an effort to cure a multiplicity of diseases was the order of the day. Along with the wholesale elimination of tonsils and of teeth we find numerous articles in the Transactions implicating the sinuses as the cause of various systemic conditions. Dean,[1] with several papers on the prevalence and significance of sinusitis in infants and small children, reported finding sinus infections in many cases of arthritis, bronchiectasis, and even chorea. He stated that while a majority of these cases were relieved by tonsillectomy and adenoidectomy, together with pediatric treatment, many required removal of middle turbinates, opening of antra, and often operation on the ethmoids and sphenoids. Later, in 1929, Dean[1] discussed the relation of diet deficiency to diseases of the sinuses in children, stressing the importance of vitamin therapy, indicating a beginning conservative trend, with attention to other and more basic causes.

During this time, papers by Faulkner,[2] Emerson,[3] and Hurd,[4] all condemned the sinuses, particularly the ethmoids, as foci of infection causing arthritis, and reported cures following operation. McGinnis[5] described what he termed "non-suppurative ethmoiditis," advocating ethmoidectomy in these cases. It is interesting to note the particular emphasis placed upon the ethmoids and the tendency to advise operation on minimal local signs and symptoms.

Berry's[6,7] papers of 1926 and 1929 shifted the target to the maxillary antrum, emphasizing the etiological factor of dental caries.

Indeed he seemed to overemphasize, as he felt that from 60 to 80 per cent of antral disease was of dental origin.

It was in this period that Leon White[8] presented his controversial paper on "Blindness from Teeth, Tonsils, and Accessory Sinuses," advocating operation in cases of retrobulbar optic neuritis "whenever x-ray studies revealed the optic foramen to be four millimeters or less in diameter." In a later paper in 1926 White[9] conscientiously repudiated his previous contention that a negative pressure in the sphenoid sinuses was a factor and reversed his attitude, at least as to operation on the sinuses. Meanwhile, Sewall,[10] always the master of surgical technique, presented his proposed operation for enlarging the optic foramen for the relief of pressure on the optic nerve, a beautiful technical procedure, but one that would be little called for.

During this period there was a tendency to consider bronchiectasis as secondary to chronic sinusitis. Dean[1] had emphasized this in his papers dealing with childhood sinus disease. In 1932 Mullin[11] reviewed this question, bringing out the fact that sinus surgery alone would not cure bronchiectasis. In the discussion, however, Faulkner[12] maintained that radical operation on the sinuses was the most conservative therapy. Five years later Goodale[13] analyzed a large series of cases showing that chronic sinusitis merely increased the chances of damage to the lungs, making them more susceptible to respiratory infections.

In view of the frequency with which allergy is encountered in conditions involving the sinuses it is rather surprising to note that not until 1929 was it accorded a place on our programs. At that meeting Emerson[14] presented his paper on "Anaphylaxis and Allergy in Rhinology." The following year Kolmer[15] discussed the "General Principles of Allergy" as a part of a symposium including papers by Weille, Hastings, and Tobey. Emerson's work was largely on cases of asthma, which he had treated by the Caldwell-Luc operation. In the discussion of his paper Coates reported the finding of eosinophils in the mucous membranes of the antra in asthmatic cases, the significance of which was not known. This is rather interesting for, although Worthin Jones had described the finding of eosinophils in the secretions of shock organs in 1846, it was left for Hansel[16] in 1940 to point out their diagnostic value in nasal cytology.

I am sure that the present day reader of these papers would be appalled at the frequency of surgical interference in the face of a paucity, indeed often a complete lack, of local signs and symptoms, and on grounds that hardly could be considered valid today. But with the widespread over-emphasis upon focal infections and little comprehension of the part played by metabolic disorders and various general systemic conditions, this is understandable. Certainly too many sinuses were operated upon, with a disregard of physiology and a poor conception of the etiology. Often the etiological sequence was reversed, the sinuses being considered the cause of some general disease, when symptoms suggestive of sinus involvement were the result of a systemic condition. Postnasal discharge, under the popular designation of "drip" had begun to achieve the dignity of a disease entity in the minds of many apprehensive patients. This was aided and abetted by the practices of certain over-eager physicians who failed to recognize the effect of dietary, endocrine, and environmental factors on an otherwise normal physiological process. The over-treated nose often became a cause of continued trouble to the patient and a source of income to the doctor.

In the earlier part of this period the most commonly performed operations were the Caldwell-Luc or the Denker, the intranasal ethmoidectomy and sphenoidectomy, and the Killian external frontal sinus operation. While various intranasal procedures, such as rasping the nasofrontal duct or the use of an indwelling tube, were employed to provide drainage for the frontal sinus, for the most part dependence was placed upon opening the anterior ethmoid cells, and upon middle turbinectomy. The earlier trephine operation, now recognized as the preferred procedure in acute conditions requiring surgical drainage, apparently had been forgotten. Discussion was often heated as to whether or not the middle turbinate should be preserved. It had not as yet achieved the sanctity of its larger neighbor, the inferior turbinate, so most often it was sacrificed.

Along with the current vogue for frequent and extensive sinus surgery came a realization of the limitations of these various procedures, together with a growing concern regarding complications such as osteomyelitis and intracranial sequelae, particularly following operations on the frontal sinus or the ethmoids. At the same time the inadequacy of intranasal surgery to effect an exenteration of the

ethmoid cells led to an increasing use of the external approach to this region.

The Killian operation had been employed largely in chronic or resistant conditions of the frontal sinus. Soon one notes an increasing dissatisfaction with the results, with recurrences at first blamed upon "incomplete removal of every vestige of infection." Mosher's pleas for the "preservation of the virginity of the nasofrontal duct" have been heard but generally given little heed. Indeed one may wonder how virginity could be preserved in the face of rape, even surgical rape.

In 1938 Furstenburg[17] presented a timely paper on the treatment of acute sinus conditions, emphasizing the hazards of extensive surgery and advocating conservative management. Crowe,[18] ten years later, advised external drainage by trephine in acute frontal sinusitis requiring surgical drainage, in order to avoid traumatizing the mucous membrane and subsequent scarring of the nasofrontal duct, as likely to lead to chronic infection.

Lynch's[19] operation, presented with the advice, "when all else fails, try this," opened the frontal sinus by complete removal of the floor and lining, as well as the ethmoid cells. This was a definite improvement and soon replaced the Killian in popularity. It became evident, however, that even with the removal of the ethmoid cells it was exceedingly difficult to maintain a patent nasofrontal duct and that with any sinus cavity remaining, as with the Lynch procedure, postoperative closure of the duct tended to recurrence of infection and possible complications. As so well stated by McNally and Stuart[20] in a study of postoperative cases, "The crux of external sinus surgery is the establishment of a patent nasofrontal duct."

The intent of this paper is to confine discussion to disease of the sinuses, per se, excluding malignant conditions and complications such as antro-alveolar fistulae and osteomyelitis of the cranial bones. It may not be amiss, however, to state that Lynch's contention that osteomyelitis could be prevented by avoiding elevation of the external periostium of the frontal bone is open to question. For, as pointed out by Furstenburg, the blood supply for the cranial bones is from the internal periostium. Decrease in the incidence of osteomyelitis was due to a better appreciation of the dangers in too early and too extensive operations in the acute stage, to emphasis upon drainage with a

minimum of surgical trauma, and, above all, to the development of chemotherapy and later antibiotic therapy.

Two later modifications of the Lynch operation have made it effective, at least in the majority of cases. Sewall's[21] use of a mucosal flap from the middle turbinate and Goodale's[22] employment of tantalum foil, or tubing, as a permanent drain should prevent closure of the nasofrontal duct and have been widely adopted.

Obliteration of the frontal sinus, the truly radical procedure to meet the demands of the resistant case, while dating back to Kuhnt's early work in 1895, would have only rare acceptance, pending the development of modern plastic surgery to overcome the inevitable deformity. This solution to the problem was first suggested by Mosher in his last years and reported by Goodale[22] three years ago.

While the Denker declined in popularity, the Caldwell-Luc operation has continued to have general acceptance for cases of chronic maxillary sinusitis requiring the external approach. But with the realization that pathological changes in the lining membrane often were reversible, and influenced by the work of Proetz,[23] Van Alyea,[24] and Goodyear,[25] more and more this operation has been effectively replaced by the intranasal antrostomy. At one time the Jansen transantral ethmoidectomy was employed when a combined procedure was indicated. While providing an improved access to the posterior ethmoid cells its disadvantages were made evident by Proetz's studies on normal antral drainage, showing the importance of preservation of the antral ostia.

Throughout these four dacades we see rays of light, searching for the basic truths so needed; in the literature, the contributions of our speakers, and in the discussions. It is interesting to note that the first paper on what might be considered a physiological subject in the Transactions for this period, was by Rockwell Coffin[26] in 1922, reporting on the atmospheric pressure in the maxillary antrum. Four years later Proetz[23] made the first of his many significant contributions in a paper on displacement, followed later by studies on nasal cilia, the minute anatomy of the sphenoid ostium, vasoconstrictors, endocrine relations, respiratory air currents in the nose, and humidity. Carmody,[27] Eggston,[28] Schall,[29] and McMahon[30] all contributed noteworthy papers on the pathology, awakening interest in this heretofore neglected area.

Indeed perusal of the Transactions reveals many valuable contributions on pertinent basic subjects during this period. In addition to those just referred to, mention should be made of Taylor's[31] work on the relations of swimming and sinusitis, Fenton's[32] studies on mucosal immunity, and the papers of Lierle and Moore[33] on the effect of drugs on ciliary activity and of Harkness[34] on endocrine imbalance. Fabricant[35] contributed his discussion of the ph factor and, as before referred to, Kolmer,[15] and later Hansel,[16] presented informative papers on allergy. These, together with Rawlins'[36] work on mesenchyme, Tremble's[37] studies on nasal cilia, and Weille's[38] discussion of virology and its relation to polypi, all have made for a better understanding of this problem.

As a result of these developments of forty years, the management of acute and chronic paranasal sinus disease has become much more effective. We have improved diagnostic facilities and more effective therapeutic agents, as well as a clearer conception of the etiology.

The majority of acute cases will respond to conservative treatment, especially if recognized early. Bed-rest, judicious use of vasoconstrictors and displacement therapy still constitute the basic treatment for acute sinusitis. Persistence of symptoms and signs, particularly if febrile, may indicate the use of definitive antibiotic medication based upon culture and sensitivity studies. However, indiscriminate use of antibiotics, especially for self-limited conditions, is open to criticism and indeed may interfere with the natural response of the patient's own defense mechanism, making him susceptible to recurrences of the infection. Antral irrigations may be indicated if roentgenograms reveal fluid levels. The resurrection of the trephine operation with the use of a small polyethylene tube, left in situ for irrigating the frontal sinus, provides an excellent means of promoting recovery in the case resistant to more conservative measures. This procedure, as well as the intranasal antrostomy, adequately covered by antibiotics, may be used to advantage when surgical drainage is required.

The realization of the frequency of allergic manifestations and the routine use of thorough diagnostic studies, including cytological examinations has resulted in less unnecessary surgery and a more rational and conservative management, carried on in co-operation with the allergist. Polypi, of course, must be removed and at times

intramural electrocoagulation of large inferior turbinates, or removal of hypertrophic posterior tips may be required to relieve nasal obstruction. Occasionally turbinotomy, submucous resection of significant septal deviations, and even operations on the sinuses may be required in particularly resistant cases or those with irreversible pathological changes, but only in combination with allergic therapy.

More definitive sinus surgery may be indicated in chronic nonallergic cases but only after thorough study, bearing in mind that the sinus condition may be only a part of some systemic disease process. A careful well-taken history, a thorough examination including all indicated diagnostic studies and consultations should be routine. Frequently the co-operation of the internist, the pediatrist, the endocrinologist and even the psychiatrist is essential in determining and carrying out the best management. This is no place for the production line, nor for the isolationist attitude.

Less radical surgery is performed today but when done is on valid grounds and carried out with greater security and less fear of lasting deformity. The Lynch frontal sinus operation with the use of the tantalum drain, or the mucosal flap, will be required at times, as will be the obliterative procedure. Even the intranasal ethmoidectomy and sphenoidectomy may be employed to advantage, although much less frequently than in the past. The Caldwell-Luc will continue to be indicated but not as often as the intranasal antrostomy. Even the middle turbinates cannot be accorded complete sanctity and at times the transantral ethmoidectomy may be the most effective means of dealing with postoperative cicatricial formation resulting in impaired drainage.

Much depends upon judgment, based upon diagnostic acumen, experience and a conscience. Our aims should be the relief of symptoms and the preservation of function as nearly as is possible; what we might term rational management.

Medicine is not an exact science, nor is it static. It is continually changing as the result of new developments, of research, and of the analyses of clinical experience. Consequently we may feel assured that the management of paranasal sinus disease will be even more effective in the coming years. Probably this will be most evident in the area of prevention. Future developments in virology may solve the

problem of the common cold. Better understanding of the autonomic nervous system may provide a more definitive approach to allergic disorders. Improvement in our environmental conditions of everyday living may serve to better protect nasal mucous membranes from excessive heat and drying, as well as dust, noxious fumes, and smog. And, if one can be sufficiently optimistic, perhaps we might look forward to a time when a more stable mental status would replace the emotional stress and tension, so prevalent today in many of our people.

The changing years may be likened to the movements of the swinging pendulum of the clock whose continued excursions back and forth to the extremities of its arc serve to mark the progress of time. In medicine these changing years may reach extremes which seem excessively radical or unduly conservative to the contemporary observer. But, as with the clock, the movements to and fro, often to seeming extremes, develop the impetus, the energy necessary for progress for a rational therapeusis.

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LII

SURGERY TO THE NASAL LOBULE

HENRY L. WILLIAMS, M.D.

ROCHESTER, MINN.

Almost from its introduction by Freer there has been dissatisfaction with the results of the complete submucous resection of the nasal septum when dislocation of the caudal edge of the septal cartilage into the vestibule has caused distortion of the vestibule and lobule.

With the Freer incision, even though it is carried down to include the periosteal compartments of the anterior portion of the septum, it is extremely difficult to work forward to release the deflected portion, especially as after fracture and dislocation it is often bound to the enveloping perichondrium and periosteum with firm adhesions. The premaxilla, vomer and maxillary crest are often pushed to one side, and this bony deformity is nearly impossible to correct through the Freer incision. Making the initial incision over the anterior dislocated caudal edge of the septal cartilage gives an improved result, but if the antero-inferior portion of the septal cartilage is entirely removed, subsequent contraction of scar tissue is likely to result in depression of the bridge of the nose (saddle nose) and retraction of the columella. Deformities of the anterior portion of the bony septum are difficult to correct. Replacement of the excised cartilage to support the tip and columella was suggested by Peer[17,18] but is difficult, and even after apparently satisfactory insertion the cartilage not infrequently becomes displaced.

Making an incision anterior to the dislocated cartilage, removing the cartilage back to the midline of the nose, then making a more posterior incision on the opposite side, and leaving a post of cartilage between the two incisions to support the cartilaginous bridge are only partly effective as these procedures do not eliminate the occasional retraction of the columella and drooping of the tip.

Metzenbaum advocated what has become known as the swinging-door procedure, in which the mucosa is elevated from one side back

to the angulation; a strip of cartilage is excised there to break the spring of the cartilage and then the dislocated anterior portion of the cartilage is replaced in its original position in the groove of the vomer and maxillary crest. This procedure is occasionally effective, but not infrequently the anterior portion of the septal cartilage will not be maintained in its new position and anterior obstruction produced by fracture dislocations of the bony portion of the septum cannot be easily corrected.

The procedure termed by Fomon the "Galloway technique" has offered some advantages; yet the transfixion incision leaves an anterior portion of cartilage to be removed. Its removal is often difficult because of adhesions, and also the formation of a pocket between the medial crura of the greater alar (lobular) cartilages in which the replaced cartilages are fixed results in an unnatural rigidity of the tip and columellar portion of the lobule.

In addition to the objections to these procedures already mentioned, the most important objection is that deformities of the lobule other than those of its medial wall produced by dislocation of the caudal edge of the septal cartilage may produce respiratory obstruction, and these cannot be corrected by any of the techniques mentioned.

THE NASAL LOBULE

Mink[13,14] was apparently the first to recognize the nasal lobule as a semidetached structure, being anatomically and physiologically separate from the remainder of the nose, and his work served to concentrate attention on its role in respiratory physiology and in respiratory obstruction. To appreciate these attributes of the nasal lobule, a description of the structure will be helpful.

Anatomy and Surgical Anatomy.[6] The external nose varies greatly as to size and shape, and certain well-defined types such as aquiline, Grecian, retroussé, negroid and the like have been described. In these various types of nose the size, shape and position of the lobule differ as greatly as do the more obvious differences in the shape of the nose as a whole.

Fig. 1.—*a* to *c*. Obstruction at lobule produced by a combination of drooping tip, dislocation of the anterior caudal border of the septal cartilage and excessive projection of the nose with overaction of the valves of Mink. *d* to *f*. Correction to the obstruction was secured by septal reconstruction, upward rotation of the lobule and reconstruction of the nasal pyramid with lowering of the projection and widening of the aperture at the nasal valve.

The relation which the breadth of the nose measured across the alae bears to the length measured from root to apex is termed the "nasal index" and is expressed thus:

$$\frac{\text{Greatest breadth} \times 100}{\text{Greatest length}}$$

In white races that index is less than 70 (leptorrhinian), in yellow races, between 70 and 80 (mesorrhinian), and in black races, more

than 85 (platyrrhinian). It may be seen that the size and shape of the lobule are critical in forming the nasal index.

The external nose forms a more or less triangular pyramid. The upper angle of the pyramid is termed "the root" and is generally separated from the forehead by a depression, and the base is perforated by the nares or nostrils. Its free angle is named "the apex" and the anterior border joining root and apex is called the "dorsum." The upper part of the dorsum which is supported by the nasal bones is named the "bridge." Each side of the nose forms an open angle with the cheek (nasofacial angle) and ends below in a mobile expanded portion, the ala nasi which forms the lateral boundary of the nostril and is limited above by a furrow, the alar sulcus. This marks on the outside of the nose the junction of the inferior (caudal) edge of the lateral nasal cartilage with the greater alar or lobular cartilage and indicates the position of the nasal valve of Mink.

The lobule[3,32] proper extends from the nostrils to the limen nasi (or valve of Mink). It is supported laterally by the lobular or greater alar cartilage consisting of a lateral and a medial crus which are continuous with each other in a rounded angle at the apex of the nose. The lateral crus is oval in shape; its upper border overrides the lower border of the lateral nasal cartilage and is attached to it by fibrous tissue which also joins it to the pyriform aperture of the maxilla. The inferior edge of the lateral crus does not descend as far as the opening of the nostril does. The rim of the nose, being there devoid of cartilage, is composed of fatty and connective tissue covered with skin. The medial crus bounds the medial wall of the nostril and lies mobile in the septum as it is separated from the anterior part of the septal cartilage by the membranous septum. The medial crura of the two cartilages are separated in front by a notch which corresponds to the apex of the nose, and the posterior (dorsal) end of each curves slightly lateralward and ends in a rounded extremity.

The interior of the lobule is divided in the midline by the nasal septum into two vestibules, the medial wall of each vestibule being formed by that part of the septum extending from the level of the limen nasi or valve of Mink to, and including, the columella. The nasal vestibule lies immediately above the aperture of the nostril on each side of the septum as an expanded area. It is bounded laterally by the lateral crus of the lobular (greater alar) cartilage and medially

Fig. 2.—*a* to *c*. Respiratory obstruction produced by drooping and flattening of tip and rounding and widening of nostrils. A septal deflection was also present. *d* to *f*. Obstruction was corrected by submucous resection, uncovering the lobular cartilages, transecting them lateral to the domes of the vestibules, suturing the medial ends together, removing 3 mm of cephalic border of the lateral crura and crosshatching the remaining portion of the lateral crura to correct their lateral bulging.

by the caudal part of the nasal septum. It is prolonged as a recess toward the apex of the nose and cephalically balloons anterior to the valve of Mink as the cul-de-sac. Interiorly the lateral wall of the vestibule is partly divided by a curved ridge. The vestibule is limited above and posteriorly by the limen nasi. The vestibule is lined by skin up to the limen nasi except on the septal aspect where the mucocutaneous junction lies but a few millimeters from the edge of the nostril.

The entire cartilaginous septum is of surgical importance in deformities of the lobule. The septal cartilage has an irregular quadri-

lateral form. Immediately below the level of the nasal bones it is continued on each side into the lateral nasal cartilage which may be looked on as its winglike expansion. In its lower two-thirds the ventral edge of the lateral cartilage is not directly joined to the septal cartilage proper but is separated from it by a narrow space filled by fibrous tissue. This separation adds to the mobility of its caudal edge which forms the valve of Mink. The relationships of the cephalic border of the lateral cartilage superiorly to the nasal bone and inferiorly to the cephalic border of the lobular cartilage are of considerable surgical importance. Both borders lies dorsal to the structures which they meet as shown by Straatsma.

Klaff has ably reviewed the surgical anatomy of the caudal border of the septum. From the floor of the nose upward the septum is formed of the premaxilla of which the ventral end is the anterior nasal spine. In a trough of the premaxilla lies the ventrocaudal aspect of the vomer and the cephalic edge of the vomer has a groove which receives the caudal border of the septal cartilage. Further posteriorly
The muscles influencing the activity of the alae are as follows:[21]

The Nasalis Muscle. This paired muscle arises from a membrane stretching over the nose which also gives attachment to the procerus muscle. The nasalis muscle is inserted into the fibrofatty tissue of the ala and the posterosuperior edge of the lobular cartilage. Its action is to lift the posterolateral portion of the ala upward and outward enlarging and rounding the nares.

The Quadratus Labii Superioris Muscle. The caput angulare originates from the processus frontalis and margo infraorbitalis maxillae and inserts into the skin of the ala nasi and sulcus nasolabialis. The caput infraorbitale takes its origin from the margo infraorbitalis maxillae and inserts at the sulcus nasolabialis. The caput zygomat-
the maxillary crest forms the caudal edge of the septum. The importance of these relationships lies in the fact that the mucoperiosteum and the mucoperichondrium are separate structures. The envelope of the mucoperiosteum about the premaxilla, vomer and maxillary crest must be entered on its antero-inferior aspect and its separation carried up to its contact with the mucoperichondrium surrounding the septal cartilage. At this line these envelopes may be divided by careful dissection in the midline into a common envelope coming from below upward as the mucoperiosteum is the thicker structure.

Fig. 3.—*a* to *c*. Respiratory obstruction at lobule produced by dislocation of the anterocaudal border of the septal cartilage and by alar collapse on inspiration. *d* to *f*. Correction was secured by septal reconstruction and reconstruction of nasal pyramid with lowering of its excessive projection and widening of the nostrils.

icum takes origin from the facies malaris ossi zygomatici and inserts into the sulcus nasolabialis. The action of these muscles is to draw the ala nasi and upper lip upward and outward, to widen the nasal opening and to deepen the sulcus nasolabialis. All the muscles influencing the alae nasi are innervated by branches of the nervus facialis.

THE PHYSIOLOGY OF THE LOBULE

Mink[13,14] stated that the nasal lobule and especially the nasal valve were of importance in respiration and that the action of the

muscles of the alae nasi influencing the nasal aperture is controlled by the respiratory centers. Mink's hypotheses have received confirmation from the investigations of Negus[15,16] who demonstrated the importance of respiratory resistance in the normal functioning of the Hering-Breuer reflex and the demonstration by van Dishoeck[28-31] of the action of the lobular muscles during the phases of respiration.

Theoretically, therefore, one might have respiratory insufficiency from lack of resistance caused by a too wide opening of the vestibule and particularly the nasal valve. This is rarely if ever seen clinically, probably because of the compensating effect of the cavernous tissues of the inferior and middle turbinates[1,2,26] and, if this fails, of the glottic chink,[15] even though, as Rohrer found, 47.3 per cent of the resistance of the respiratory system lies in the nose and less than 7 per cent lies in the glottis.

Attempts have been made to attach greater physiologic importance to the effect of excessive resistance on nasal obstruction. For instance, Killick stated that the important factors which bring about respiratory failure from breathing through an excessive resistance are fatigue of the respiratory muscles and retention of carbon dioxide.

Davies, Haldane and Priestley stated that if resistance to natural breathing is thrown in for purely mechanical reasons, respiration will be slowed down at first. In a short time, however, the alveolar carbon dioxide pressure will rise. As a consequence the driving pressure, inspiratory or expiratory, will become greater and this will tend to restore the original rate. But the depth of breathing also will increase, since the degree of distention or collapse of the pulmonary alveoli at which the phase of respiration reverses will increase. The net result will be that breathing becomes both deeper and slower than before the resistance began. With excessive resistance the phase of slowing and deepening of breathing is followed sooner or later by a phase in which the rate of breathing increases and the depth diminishes. The significance of this change is that shallow breathing causes anoxemia, and anoxemia causes shallow breathing. The body is in a vicious circle which if not broken must inevitably cause death.

Sternstein and Sternstein and Schur found that the nasal respiratory resistance could be increased from 3.25 to 6.50 mm of water

Fig. 4.—*a* to *c*. Respiratory obstruction at vestibule produced by turning of caudal margin of lateral cartilages inward toward lumen of vestibules. There was also a moderate degree of drooping of the tip. *d* to *f*. The obstruction was relieved by intracartilaginous incisions, a submucous elevation of the caudal border of the lateral cartilage and excision of the inturning portion. The vestibular skin and the nasal mucosa then were sutured over the defect.

without the patient's being aware of it. He found that patients become subjectively aware of increased nasal resistance at an average of 8.25 mm of water. It is possible, therefore, that deleterious effects might be caused by nasal respiratory obstruction, but such effects must be so limited as to make them rarely observable clinically.

The physiologic effects of nasal respiratory obstruction have been reviewed and summarized by Uddströmer[27] in his monograph on

nasal respiration. He defined nasal respiratory insufficiency as the state in which it is impossible or difficult for the individual to procure through the nose alone the amount of air necessary for satisfactory pulmonary ventilation. If this occurs in repose, the insufficiency is absolute; if it does not occur until demands are raised, which are well endured by a nose functioning normally, the insufficiency is relative.

As far as nasal respiratory obstruction having an effect on the physiology of respiration as a whole, Uddströmer[27] was certain of but two points. The first was that the greater the oral part of respiration, the greater is the total volume. This is an attempt of the organism to compensate for defective nasal respiration. He stated that Yosa had proved that during exertion mouth breathing tended to produce an earlier dyspnea and hence a quickly rising exhaustion. Uddströmer's second point was that in certain dusty trades oral breathing may be considered detrimental.

INDICATIONS FOR OPERATIONS ON THE LOBULE

Although both a decrease and an increase in normal nasal resistance to respiration may produce harmful physiologic effects, it is not probable that much nasal surgery is done to relieve such effects. That these deleterious effects are theoretic rather than actual in most instances is shown by the fact that individuals who grow up with nasal respiratory insufficiency do not evidence any notable tendency to early exhaustion on effort. It seems impossible to demonstrate any physiologic effect in most patients who come to the otolaryngologist with the complaint of nasal obstruction. It seems wiser, therefore, to admit that most nasal operations are done to secure subjective relief of subjective nasal obstruction rather than argue that restoration of nasal function will have a general beneficial effect on the organism, at least one that is obviously apparent.

Proetz stated deformities of the lobule which may produce subjective symptoms are as follows:

First, too narrow nostrils, especially those that tend to collapse on inspiration, may cause such symptoms. If this is due to lack of development of the alar musculature or inco-ordination of the muscles owing to defects in innervation from the respiratory center, little

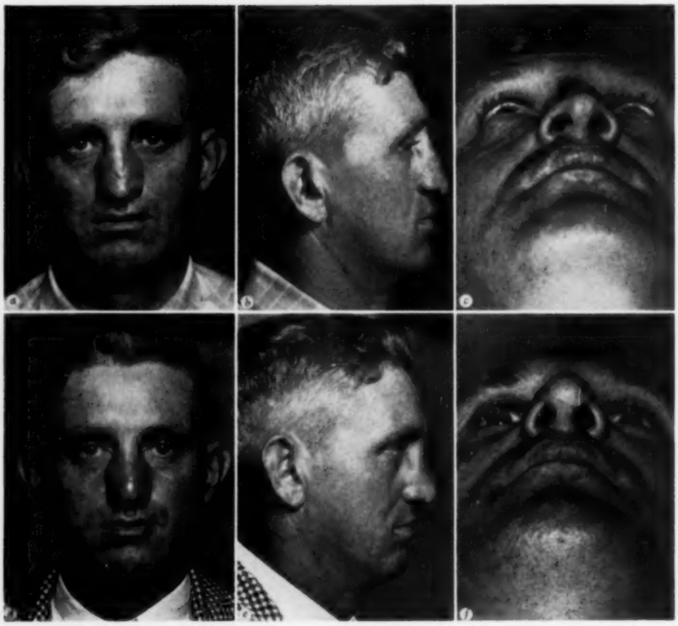

Fig. 5.—*a* to *c*. Obstruction at the lobule was produced largely by extreme drooping of the tip. There was also a moderate dislocation of the anterior caudal border of the septal cartilage. *d* to *f*. Correction was secured by septal and nasal reconstruction and upward rotation of the lobule.

can be done to correct it. If this defect is produced by very long and narrow nostrils in a nose with excessive projection from the face, decreasing the projection and flattening of the base of the nose will give a measure of relief.

Second, the lobule may be deformed and fail to direct the stream of air properly. Such a deformity of the lobule is ordinarily produced by dislocations of the caudal end of the septum, as Metzenbaum pointed out.

Third, the usual relationship between the lateral nasal cartilage and the greater alar (lobular) cartilage may be altered and, instead

of the caudal edge of the lateral cartilage lying dorsal to the lobular cartilage, the relations may be reversed. This allows the cephalic border of the lobular cartilage to bend down into the air stream causing obstruction. This may be relieved by excising the cephalic downcurving border of the lobular cartilage.

Fourth, the nasal valve may be overactive because of too great length and weakness of the caudal border of the lateral nasal cartilage. This is especially likely to occur in noses with great projection from the face and may be corrected by reduction of the projection of the nose.

Cottle[3] added a fifth cause of lobular obstruction in which the caudal portion of the lateral cartilage may curve inward toward the septum producing a marked narrowing of the aperture of the nasal valve. This may be corrected by submucous dissection and resection of the caudal (lower) border of the lateral cartilage or by breaking the spring of the cartilage by suitable cross incisions.

Sixth (Proetz), the obstruction may be produced by a downturning nasal tip. Sercer noted that individuals, in whom the tip of the nose drooped as a result of trauma, after elevation of the tip of the nose, experienced not only esthetic improvement but also improvement in nasal respiration. He stated that the three most important anthropologic types of nasal profile were those in which the caudal edge of the septum forms a right angle, an obtuse angle or an acute angle with the upper lip. In these types the nasolabial angle, the nares and the nasal chambers are in harmony, and breathing is free and unobstructed. But if in one of these types pathologic causes provoke a change in the relative position of the nasal orifice, functional difficulties will appear. This is owing to the fact that the direction of the inspired air through the nasal chambers depends in part on the position of the nostrils and nasal lobule relative to the nasal chambers.

These then are the conditions causing nasal respiratory obstruction and an integrated operative technique which is capable of correcting them at the same sitting must be used. It must be recognized also that deformities of the nasal vault which coexist with lobular deformities may prevent the complete correction of deformities of the lobule and must also be taken into consideration.

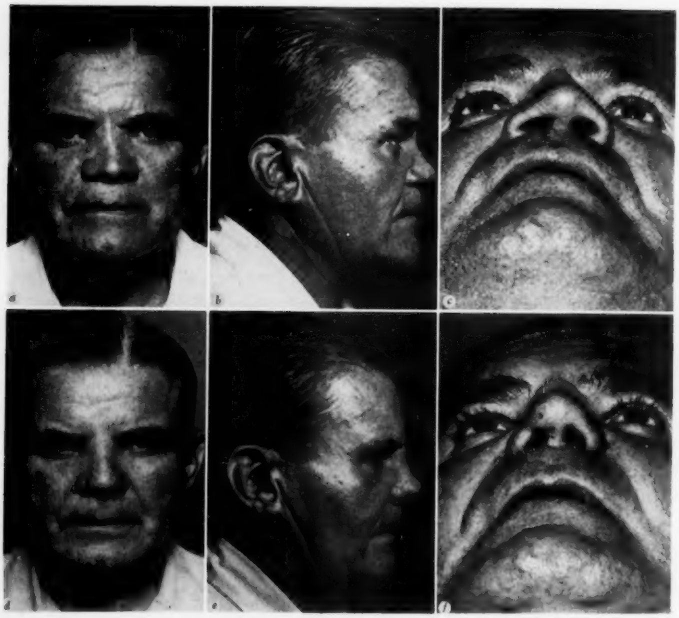

Fig. 6.—*a* to *c*. Obstruction produced by extreme flattening and widening of nasal lobule. *d* to *f*. Correction was attained by incision through alar-facial groove with removal of wedge of tissue, baring the lobular cartilages and transecting them lateral to the domes, and by upward rotation of the lobule.

It is also evident that correct diagnosis of the cause or causes of lobular respiratory obstruction is an important matter in the selection of the technical variations that may be necessary in an individual case. Diagnosis is a matter of careful observation and can be learned only by experience.

THE TECHNIQUE FOR RELIEVING LOBULAR RESPIRATORY INSUFFICIENCY

Cottle[4,5] has garnered the fruits of the efforts of several generations of rhinologic surgeons and winnowed the wheat from the chaff.

He has united the best technical procedures from many surgeons into a complete, flexible and easily applicable surgical technique.

Septal Dislocation (Fig. 1). The septal incision is made on the side closest to the surgeon's master hand. The columella is drawn to the opposite side because this puts the caudal extremity of the septal cartilage in the nearest vestibule and stretches and tenses the mucosa on the near side of the septum. An incision is then made through the mucosa and perichondrium down to the cartilage 3 to 4 mm posterior to the caudal edge of the septal cartilage. The anterior portion of the mucosa and perichondrium are then elevated forward and around the caudal edge of the septal cartilage, and the mucosa and perichondrium are elevated from the side of the cartilage opposite to the original incision. The mucosa and perichondrium are then elevated from the same side of the incision. With a pair of iris scissors beginning at the nasal spine the tissues in front of the premaxilla are elevated, the nasal spine is bared of fibrous adhesions, and the periosteum is elevated from the premaxillary wings, vomer and maxillary crest. The elevations of the perichondriums and the periosteums are then connected. This gives full access to the septal space, the cartilage may be removed and again replaced to support the tip and prevent adhesions from contracting and pulling up the columella or pulling down the bridge of the cartilaginous portion of the nasal dorsum. Anterior deflections along the floor formed by fracture and dislocation of the bony portion of the septum may be chiseled off. The anterior nasal spine must be carefully preserved because it forms the anchor for the dorsal end of the columella, fixing it and helping to prevent retraction of the columella. It also anchors the dorsal end of the columella in upward rotation of the lobule which will be described later. Deflected and distorted portions of the cartilaginous septum may be removed, but straight pieces in the midline may be left in situ. At the termination of the operative procedures a straight and suitably shaped piece of the septal cartilage is secured, its caudal edge placed in the pocket from which the caudal edge of the septum was originally removed and the remainder is placed between the flaps of septal mucosa and the perichondrium. The original incision is drawn together and the cartilage is fixed by sutures.

Deformities of the Lobular Cartilage. Incisions are made within the nose through the skin paralleling the caudal edge of the lobular cartilage to the skin of the external nose (Fig. 2). The integument

Fig. 7.—*a* to *c*. This illustrates the difficulty of securing relief of nasal obstruction when the deflection is maintained by a deformity of the bony bridge. In this case obstruction was also produced by collapse of the ala on the right. *d* to *e*. Relief of obstruction was secured by septal and nasal reconstruction decreasing the forward projection of the nose with slight flattening and upward rotation of the lobule.

is elevated from the ventral and lateral surfaces of the lateral crura and the dome, and the medial crura are bared sufficiently for manipulation. The cartilages are cut across, allowing the medial crura and domes to spring up or to be sutured to each other if further accentuation of the nasal tip is desirable. The lobular skin may be separated from the lobular cartilage if it is desirable to spare scarring or it may be incised along with the cartilage. If the cephalic edges of the lateral crura are in abnormal relation to the caudal edges of the lateral cartilages with the cephalic edges of the lateral crura bending inward toward the lumen of the lobules and thus causing respiratory

obstruction, the inbending edges can be excised and the obstruction eliminated.

Obstructions Caused by the Caudal Edges of the Lateral Cartilages. These are of two kinds (Fig. 3). The first is caused by an excessively long and thin caudal edge of the lateral cartilage. This is seen in noses with excessive projection from the face and may be corrected by lowering the bridge of the nose and removing a portion of the ventral aspect of the lateral cartilages, thus shortening the valve and causing it to make a nice obtuse angle with the septum.

The second obstruction (Fig. 4) caused by the lateral cartilages is produced by the curving of the thin caudal borders into the nasal lumen.

After the lateral cartilages are bared by the Joseph incision, their dorsal surfaces may be uncovered by a submucous resection of the nasal mucosa. The deformed edges may then be excised. If the lateral cartilages above the inturned edges have an abnormal ventral bulge, this may be corrected by crosshatched incisions in the cartilages which allow them to be shaped to an approximation of their normal contour (Fig. 4).

Correction of Obstruction From Overhanging Tip (Fig. 5). This requires upward or cephalic rotation of the lobule. For this maneuver the preservation of the anchor of the anterior nasal spine is most important. After removal of the septal cartilage, and after the intracartilaginous incisions and uncovering the bones of the dorsum of the nose, the amount of elevation of the tip necessary to overcorrect the drooping slightly is estimated, and a wedge-shaped piece is cut from the cephalic border of each lateral cartilage, the base of the wedge being at the junction of the lateral cartilage with the septum, and the apex toward the ventral termination of the cephalic border. After these wedges are removed, the vestibular skin is sutured to the mucosa lying posteriorly to help maintain the elevated position of the lobule. In the replacement of the anterior portion of the removed septal cartilage, care is taken to make a proper angle between the cephalic edge of the implant from the anterior nasal spine to the tip and the portion that runs along the floor of the nose before fixing it in position. The elevated position of the tip is further maintained during the postoperative period by the application of an external splint of adhesive plaster.

Obstruction Produced by Ventral Displacement of the Tip and Broadening and Flattening of the Alae. This deformity results in deformity of the passage through the vestibule which as Proetz has shown directs the inspired air into a thin sheet between the septum and middle meatus so that the air stream is not properly directed. This causes eddies that produce obstruction to nasal breathing at the lobule. In addition to elevation of the tip and rotation of the lobule narrowing of the lateral expansions of the alae may be required. This is accomplished by incisions along the alar-facial groove which pass into the lumen of the lobule. Then a suitable wedge-shaped portion of the foot of the lobule along the caudal edge of the incision is removed and the edges of the incision are sutured (Fig. 6).

Other Conditions. Finally it must be remembered that deformities of the bony and cartilaginous vault (Fig. 7) are capable of maintaining deformities in the region of the lobule, and when this is the case, the entire external nasal deformity together with deformity of the septum and lobule must be corrected in one procedure in which all the separate technical maneuvers are collected into one complete procedure. Only in this way will the ultimate in subjective and physiologic relief to lobular respiratory obstruction be corrected.

MAYO CLINIC

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LIII

CARCINOMA IN SITU OF THE LARYNX: A TEN YEAR STUDY OF ITS HISTOPATHOLOGICAL CLASSIFICATION, PROGNOSIS AND TREATMENT

H. Russell Fisher, M.D.

(By invitation)

and

Alden H. Miller, M.D.

Los Angeles, Calif.

Carcinoma in situ of the larynx continues to present problems to the laryngologist. Five years ago we gave our experiences over a five-year period with 13 patients in whom carcinoma in situ of the larynx was their only presenting lesion.[1] We attempted to begin to answer a series of questions as to the pathogenesis of this lesion, the criteria for its identification, the invasive potential that might be anticipated, and the most appropriate treatment for it. At that time we concluded that full elucidation of this subject would require the study of cases over a long period. It is our purpose to continue this study, which has now passed the ten year mark.

This report concerns 48 patients with carcinoma in situ of the larynx, seen from 1947 to 1958. The majority were males, only seven being females. Their average age at the time of our first recognition of this condition was 55 years for the males and 44 years for the females.

All the patients in this series have had histopathologically proven carcinoma in situ, without invasive carcinoma, when the diagnosis was first made. We have previously specified the essential histological criteria used to identify this lesion.[1] In carcinoma in situ the epi-

From the Departments of Otorhinolaryngology and Pathology, School of Medicine, University of Southern California, and the Los Angeles Eye and Ear Hospital.

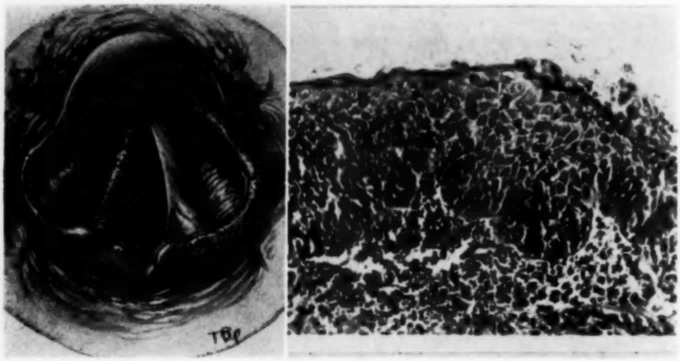

Fig. 1.—Patient D.A. a) The entire cord affected by a large, uniform red swelling which histologically b) exhibits a predominantly basal type pattern.

thelium assumes a malignant morphologic pattern, without extension of the epithelial proliferation below the basement membrane. The chief morphologic features are lack of cellular differentiation, hypercellularity, anisonucleosis, macronucleosis, hyperchromatism and abnormal mitosis. The variability of microscopic patterns satisfying these criteria has led one of us to attempt to classify carcinoma in situ into three pattern types.[2] Following this approach we have reexamined the tissues from our patients in an effort to test the possibility of correlating clinical signs, indications for treatment, and invasive potential with the microscopic pattern of the lesion.

HISTOPATHOLOGIC CLASSIFICATION

The three histopathologic patterns of carcinoma in situ into which our material appears to fall have been designated as: 1) basal, 2) squamous and 3) Bowenoid. In the basal type there is crowding of undifferentiated basal type cells throughout the entire thickness of the epithelial layer. In the squamous type, which has been most frequently encountered, the cells tend to partially differentiate as squamous elements above the basal layer. In the least frequently seen variety, the Bowenoid type, the epithelial pegs are exaggerated and

Fig. 2.—Patient F.F. a) The middle of the cord is involved by a red nodular swelling, flecked with minimal leukoplakia. b) Predominantly bowenoid pattern carcinoma in situ.

frequently festooned with expanded, squamoid cells developing in the basal layer. The 48 patients included 7 in which the basal pattern was pure. The majority were of the squamous type at onset. Only four patients exhibited the Bowenoid type of carcinoma in situ. When there was an opportunity to obtain repeat biopsies of individual cases it was found that basal and squamous types were often intermixed, or alternated.

CLINICAL FINDINGS

As in our previous report we have been unable to define a characteristic or distinctive clinical picture on laryngoscopy, indirect or direct. Leukoplakia was the most frequently seen pathological change; it was present in 25 patients. This leukoplakia varied from single plaques over one-third of a cord to complete involvement of both cords. It was bilateral in seven cases. There was only injected swelling, localized or diffuse, of one cord, in ten patients. Carcinoma in situ was found in three patients in what appeared to be typical contact ulcer granulomas. In two cases the larynx exhibited only the polypoid pads of chronic hypertrophic laryngitis. One patient appeared to have two typical vocal nodules; both contained carcinoma in situ. We do not believe that there is a typical picture which

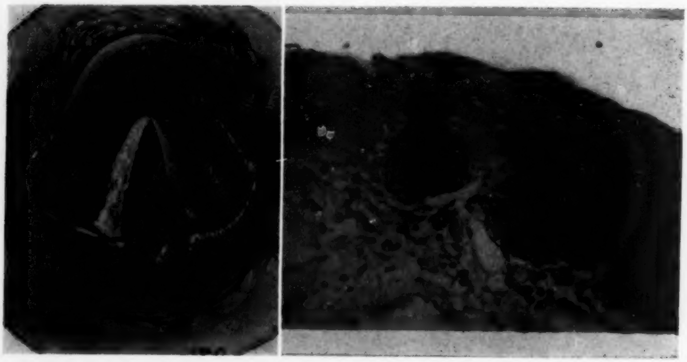

Fig. 3.—Patient H.B. a) Leukoplakia is prominent and extensive. b) Squamous type carcinoma in situ near the junction with columnar epithelium.

strongly suggests only carcinoma in situ. The lesion most suggestive is a thick, shaggy leukoplakia, superimposed on an irregularly thickened and reddened mucosa.

This variability in the clinical picture might be anticipated when the variability of the cellular structure is considered. We were able to correlate clinical and microscopic findings in 38 cases. In our material there appears to be a strong correlation between the clinical identification of dense leukoplakia and the microscopic occurrence of the squamous type of carcinoma in situ (Fig. 3). This was noted in 16 patients. The basal type pattern was most often encountered (eight times) in those patients whose lesions were of the injected, swollen variety without leukoplakia (Fig. 1). When the clinical picture was mixed the histologic pattern was also mixed with surprising regularity (Fig. 4). Leukoplakia did not appear to be associated with the few cases of the Bowenoid pattern in our collection (Fig. 2).

MANAGEMENT

As in our first five years of experience with this disease, the choice of treatment has been predicated on the site and extent of the

lesion as well as the procedure used in first making the diagnosis. The leukoplakic lesions were often completely stripped for diagnosis. If the leukoplakia was small in extent and seemingly completely removed no further treatment was then instituted. If residual or recurrent carcinoma in situ was proven in the same limited lesion a laryngofissure operation was performed. When carcinoma in situ was found extensively or bilaterally in either the original or in subsequent biopsies, x-ray therapy was usually employed. When only minimal focal carcinoma in situ was found, even in extensive leukoplakia, complete stripping was performed as the initial treatment.

The nonleukoplakic lesions were usually limited in extent and were treated in the same way as the small leukoplakic lesions. Two patients with diffuse injected swelling of all of one cord received x-ray therapy. X-ray treatment was also used in those cases in which repeated reappearance of carcinoma in situ was proven after repeated strippings or removals.

In two patients with nonleukoplakic lesions, biopsy alone removed all detectable carcinoma in situ.

RESULTS OF TREATMENT

Sixteen patients received stripping only. Four of these subsequently developed invasive carcinoma. Three patients have had a clear larynx for six years after stripping. The other nine have remained clear for from one to three years.

Laryngofissure operations were performed on eight patients. None of these have developed invasive carcinoma. Three have been free of disease for six, seven and nine years, while the remaining five have been clear for one and four and one-half years.

Twenty-four patients were treated by x-ray. Invasion occurred in six of these. Three are nine year cures; seven more are from five to seven year cures. The remaining 13 patients are clear of disease to date. There has been one death.

Histopathological classification into types of carcinoma in situ has been in retrospect, and has not been used up to now as the basis of choice for therapy.

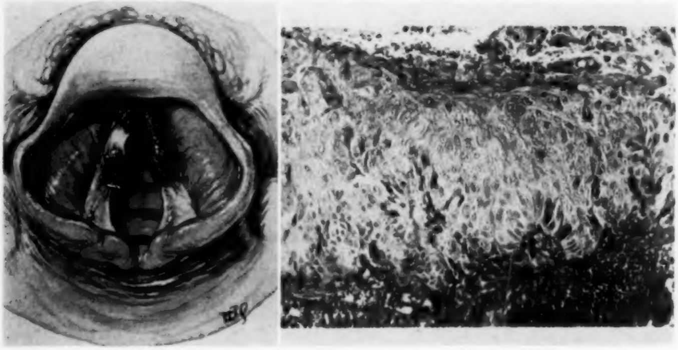

Fig. 4.—Patient S.K. a) Bilateral lesion of mixed appearance, with leukoplakia between zones of red swelling on the right cord. b) A mixed pattern, combining the features of squamous and bowenoid types of carcinoma in situ.

THE DEVELOPMENT OF INVASION

The most significant biologic feature in this study is that 10 of the 48 patients with carcinoma in situ developed invasive carcinoma despite treatment. Six developed invasive carcinoma following x-ray therapy with an average interval of four years and one month; and four exhibited invasion after stripping, with an average interval of one year and five months. The development of invasive carcinoma after an appreciable interval of time, in a lesion originally recognized only as carcinoma in situ, is a strong argument in favor of the basic malignant nature and potential of carcinoma in situ.

There appears to be an interesting correlation between the histologic typing of carcinoma in situ and the subsequent development of invasive carcinoma. Nine of the ten cases of invasion developed in lesions originally identified as of the squamous type when in situ. One instance of invasion has been detected in the nine cases of pure basal type carcinoma in situ. This would suggest that the squamous type represents the more advanced and more aggressive variety of carcinoma in situ. From another point of view, one might appropriately question the true malignant potential of the basal variety as

recognized in this study. Basal type carcinoma in situ, when associated with or followed by squamous type carcinoma in situ, has eventuated in recurrence and invasion. Also, the basal type of carcinoma in situ occurring in the cervix uteri has been associated with a high grade of malignant invasion. These features persuade us that the basal type represents a true variant of the condition understood as carcinoma in situ.

In the four cases in which invasion developed following stripping, two were treated with x-ray and two with laryngofissure operation. These patients are seemingly clear of disease after two, six, nine and 36 months. In the group of six patients initially treated with x-ray, and followed by invasion, one was successfully controlled by laryngofissure operation and five required laryngectomy. Of this group of laryngectomized patients, one subsequently developed cervical metastasis. Following a radical neck dissection, there was progressive metastasis causing death. This is the only death due to progressive malignant disease in this series. One other patient died, free of disease, from coronary thrombosis.

SUMMARY

1. A series of 48 patients having an initial lesion of carcinoma in situ of the larynx, collected over a ten year period, has been presented.

2. Carcinoma in situ of the larynx can apparently be recognized in three relatively distinct histopathologic types: the basal, the squamous and the Bowenoid.

3. There is no single, pathognomonic clinical appearance of this disease.

4. Leukoplakia is the most common clinical finding, and occurs in the squamous type of carcinoma in situ.

5. Treatment by stripping, laryngofissure or x-ray therapy has been individualized on the basis of extent of the lesion, method of original diagnosis and the development of recurrence. The laryngofissure operation has been successfully employed for relatively small unilateral lesions. X-ray, used in extensive and bilateral lesions, has obviated the need of laryngectomy in 17 of 23 patients.

6. Ten patients developed invasive carcinoma. This supports the widely held belief that carcinoma in situ has true malignant potentialities. The squamous type of carcinoma in situ appears to be most intimately related with the tendency toward subsequent invasion despite treatment.

500 South Lucas Ave.

We wish to express our appreciation to Drs. L. J. Barnes, C. Blanchard, Jr., S. J. Brockman, H. H. Burston, H. W. Fishler, A. E. Solomon, and J. W. Wall for permission to include their cases and for pathological material.

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LIV

BRONCHOSCOPIC FINDINGS IN TUBERCULOUS CHILDREN

(A FIFTEEN YEARS' STUDY)

D. E. S. WISHART, M.B.†

AND

J. B. WHALEY, M.D.
(By invitation)

TORONTO, CANADA

Primary pulmonary tuberculosis in children has long been recognized to have accompanying bronchitic changes in a not infrequent number of cases.[1] This endobronchial tuberculosis is seen in children of all ages, but is commonest in the younger age group and is found frequently in babies. The youngest infant in our series was four months old. The bronchial involvement usually occurs early in the course o fthe tuberculous disease.

This report on the bronchoscopic findings in children with endobronchial tuberculosis covers a period of 15 years from 1943 to 1957 at the Hospital for Sick Children, in Toronto. The cases were all active ones, and were under the care of Dr. Gladys Boyd, Chief of the Chest Service at the hospital during that time. Bronchoscopic examinations and bronchograms were carried out when she requested them.

Although this series began in 1943, much earlier bronchoscopic examinations of tuberculous children had been carried out at our hospital, one being as early as 1930 and another in 1931. Both of these cases had lobectomies later.

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† Deceased.

From the Department of Otolaryngology of the Hospital for Sick Children, Toronto, Canada, and the Department of Otolaryngology of the University of Toronto, Toronto, Canada.

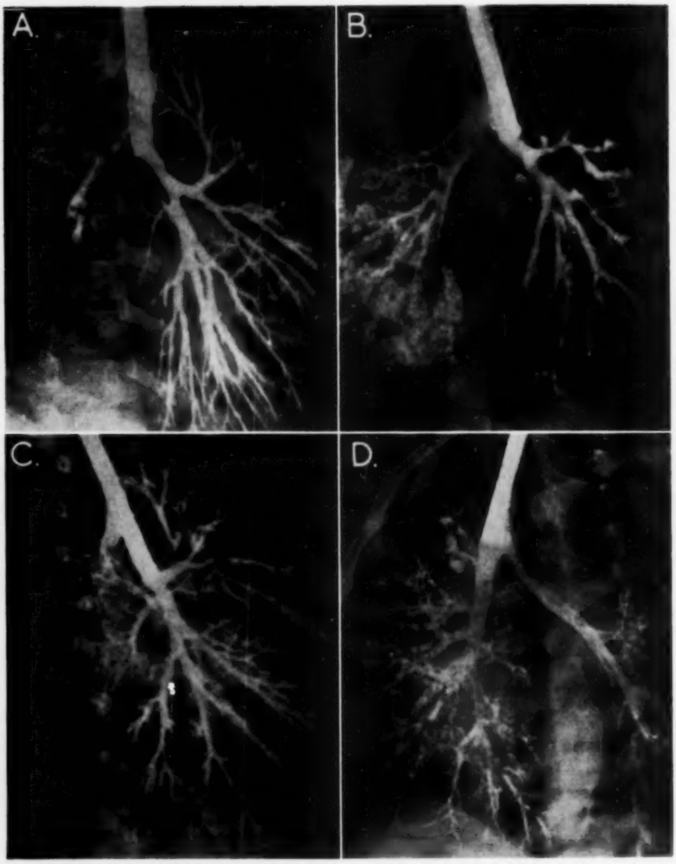

Fig. 1.—A. Normal left lung. B. T.B., bronchiectasis. Typical "flagellate" effect. Dilated proximal part of bronchi and normal or narrowed distal part. C. Constriction of bronchus to left apical posterior lobe. D. Bronchiectasis right upper lobe.

TABLE I

PRIMARY TUBERCULOUS BRONCHITIS AND BRONCHIECTASIS

CASE	AGE	BRONCHOSCOPIC FINDINGS			
1. C.G.	5	*Jan. 1950.* Much thin secretion. Area of ulceration R.M.B.	*May 1950.* Little secretion - more rt. side. Ulcer still in R.M.B. just below carina. Less inflamed.	*Oct. 1950.* Fair amt. of secretion R.M.B. which is reddened. No ulceration.	*Nov. 1950.* Fair amount of secretion sucked out. Rt. Brg. - normal.
2. M.D.	4	*May 1950.* Little secretion. M.M. healthy except small ulcer at terminal bifurcation of R.M.B. Bleeds easily.	*Oct. 1950.* Little secretion - R.M.B. red but no ulceration.		
3. T.M.	8 mos.	*1945.* Frothy mucus - greyish color R.M.B.	*Oct. 1951.* Heavy white muco-pus R.M.B. Mucosa red and swollen.	*Nov. 1951.* Brg. - R.U.L. does not fill. Stenosis 1 cm from M.B. Looks like lobe with tb cavities.	*Dec. 1951.* R.U. lobe resected.
4. I.C.	6	*July 1952.* A little whitish grey secretion. No other abnormality.	*Jan. 1953.* Constriction rt. U.L.B. Brg. shows bronchiectatic changes in R.U.L.		

ABBREVIATIONS

BR.G.	Bronchogram	L.L.L.B.	Left Lower Lobe Bronchus	R.L.L.B.	Right Lower Lobe Bronchus
L.M.B.	Left Main Bronchus	R.M.B.	Right Main Bronchus	M.M.	Mucous Membrane
L.U.L.B.	Left Upper Lobe Bronchus	R.U.L.B.	Right Upper Lobe Bronchus	L.L.L.	Left Lower Lobe
L.	Lingula	R.M.L.B.	Right Middle Lobe Bronchus	R.L.L.	Right Lower Lobe

5. D.J.	4	*Apr. 1952.* Mod. amt. frothy secretion. Rt. side mucous.	*June 1952.* Greyish secretion R.M.B. constricted. R.M. lobe contracted. Brg. R.M.L. small and bronchi collapsed.	*Apr. 1953.* R.M.L. bronchi collapsed but fill well. Mod. amt. of frothy mucoid material.	*June 1953.* Rt. middle lobe resection.
6. E.R.	3	*June 1951.* Mucous membrane R.M.B. Thin greyish white secretion.	*Jan. 1952.* Bronchi normal Brg. - R.U.L. bronchiectasis.	*June 1952.* Red m.m. rt. side. *Brg.* R.M. lobe bronchi irregular and dilated. Terminal bronchioles blocked. U. & L.B. normal.	*Jan. 1953.* Small amt. of muco pus. Red throughout. Sputum still +.
7. E.C.	11	*Sept. 1944.* Mod. amt. sticky secretion. No gran. nor ulcer.	*Nov. 1945.* General congestion Rt. M. & L. bronchi. Rt. Brg. - bronchiectasis.	*Feb. 1946.* Much pus. Constricted bronchus R.M.L. bronchiectasis.	
8. H.K.	17 mos.	*May 1951.* Sticky secretion. Constriction R.U.L.B.	*May 1951.* Brg. Cylindrical dilation and thickening R.U.L. bronchi.	*1952.* Rt. upper lobe resection.	
9. C.C.	14 mos.	*May 1953.* Mucous memb. red both main bronchi.			
10. M.R.	5	*May 1953.* Excess yellowish grey secretion R.M.B. No ulcers or granulations.			
11. T.P.	2	*Oct. 1953.* Mucopurulent secretion. Still collapse R.M.L. Bronchi constricted. Narrowing R.M.D.	*June 1946.* Refuses bronchoscopic. R.M.L. collapse but no symptoms.		

TABLE I (Continued)

CASE	AGE	BRONCHOSCOPIC FINDINGS			
12. A.B.	3½	*Mar. 1952.* Fair amount secretion. Greyish white R.M.B. ulceration - no granulations R.U.L.B. bled easily.			
13. J.W.	8 mos.	*June 1951.* A little thin secretion - grey color. Bronchi healthy.	*May 1952.* Mucosa red. Brg. (l.) normal.	*Nov. 1952.* Bronchi look alright but rt. bronchogram showed bronchiectasis R.U.L.	
14. R.N.	6	*Apr. 1950.* Bronchial mucosa red. Thin muco pus especially right side.	*Oct. 1950.* Slight mucoid secretion. Bronchi appeared normal.	*May 1951.* Larynx red. Carina red. R.M.B. small ulcer which bled easily. Brg. bronchiestasis R.M.L.	*June 1951.* Thin secretion. No obstruction.
15. Y.W.	1	*July 1952.* Mod. secretion. Granulation R.M.B. - anterior wall. Some removed. Profuse bleeding.			
16. P.C.	9	*Oct. 1951.* Heavy blood stained secretion from L.M.B. Thin secretion R.M.B. Redness both sides. No granulations nor ulcers.	*Mar. 1952.* Heavy blood-stained secretion trachea and both main bronchi - more right side. No granulations nor ulcer.	*Apr. 1952.* Sticky secretion-bled easily. R.M.B. No ulcer. Brg. (Rt.) Apical branch R.U.L. bronchus stubby dilation.	

17. R.C.	7	*Mar. 1952.* Nothing much seen but R.M.B. did not fill. Brg. R.M.L. does not fill.	*Sept. 1952.* Fairly large amount of thin grey secretion. Nothing else seen.	*May 1953.* L.M.B. red. Brg. shows bronchiectasis in lingula only.
18. R.B.	7	*May 1943.* Minimal secretion L.M.B. Greyish white color.	*Feb. 1946.* Stenosed bronchus L.L.B. Post, division L.M.B. narrow and thickened.	*Aug. 1946.* Considerable muco purulent secretion l. side.
19. J.C.	7	*Feb. 1943.* Much purulent secretion. Hemorrhagic bronchial mucosa.	*Oct. 1943.* Still thick pus. Rt. middle lobe bronchiectasis.	
20. V.W.	3½	*Apr. 1951.* Mucous membrane L.M.B. red and swollen. Muco purulent secretion from this area.	*Aug. 1951.* Muco-purulent secretion R.M.B. clear. L. lower lobe bronchus still red and swollen.	
21.	5	*Jan. 1946.* Mucous membrane red rough. White secretion. R.L.L.B. Rt. Brg. Bronchiestasis R.L. and M. lobe.	*Sept. 1946.* Thick mucus. L. Brg. - normal.	*Oct. 1946.* Rt. M. and R.L. resected.
22. W.T.	13 mos.	*May 1948.* Large amount of mucoid secretion. No other abnormalities.		
23. G.W.	2½	*Feb. 1953.* Blood stained secretion. L.M.B. - mucosa red. L. Brg. Sl. bronchiectasis L.L.L.	*June 1953.* Moderate amount muco-purulent secretion. Some definite redness of m.m. Brg. (rt.) normal.	

TABLE I (Continued)

CASE	AGE	BRONCHOSCOPIC FINDINGS		
24.	3½	Slight injection. No granulations. Rt. Brg. - dilated rt. upper lobe bronchi.	*Mar. 1952.* Rt. upper lobe resected - no pathology found. No organisms grew. Abnormal systemic bl. vessels.	
25. M.T.	11	*Jan. 1950.* Heavy frothy material from trachea. Both main bronchi red and bled easily. Muco-pus and caseous material both M.B.		
26. H.B.	2	*Dec. 1949.* L.M.B. healthy. R.M.B. red and small ulcers. More secretion of grey color from R.M.B.		
27. P.C.	13	*May 1948.* (Miliary TB). Great deal of muco-pus. Redness posterio-lateral wall R.M.B. 2 shallow ulcers same area.		
28. G.G.	2	*Oct. 1951.* Moderate greyish secretion M.M. and openings normal except redness.	*Feb. 1952.* A little thin secretion. Most R.L.L. Brg. Constricted bronchi. Contracted R.L.L.	*June 1953.* X-ray still shows shrunken R.L.L.

29. E.R.	3	*June 1952.* Slight thin secretion. Red mucosa R.M.B. Brg. irregular dilated bronchi R.U.L.	*Jan. 1953.* M. M. red. Bleeds easily. Small granulation R.U.L.B.	
30. S.M.	2	*Dec. 1951.* Main bronchus clear. Very little secretion. No obstruction.	*Jan. 1952.* M. M. Red R.U.L.B. Small granulation. No caseous material. Bled easily.	*Dec. 1952.* Rt. upper lobe resected.
31. L.M.	3½	*Apr. 1951.* No acute signs L. Brg. - showed cronchiectasis l.l.l. and lingula.	*May 1951.* R. Brg. normal except irregularities in post, basal division of R.L.L.	*June 1951.* Resection of L.L.L. and lingula.
32. H.G.		L.L.B. thickened and granular. Partial obstruction. Brg. - l.l. bronchiectasis and lingula.	R. Brg. normal.	L. lower and lingula resected.
33.	3	*Mar. 1952.* A little thin secretion. Rt. Brg. - dorsal bronchus in upper L. constricted and dilated beyond this.		
34. E.L.	3½	*Apr. 1952.* L.M.B. clear. R.M.B. ulcer at entrance to R.U.L. Bled freely.		
35. V.L.	8	*Mar. 1952.* Fair amount thin grey secretion both sides. Red R.M.B. - possible ulcer. No gran.		

TABLE I (Continued)

CASE	AGE	BRONCHOSCOPIC FINDINGS		
36. H.C.	14 mos.	*May 1951.* Larynx and M.B. thin secretion. Increased redness L.M.B.	*Dec. 1951.* A little muco-purulent secretion L. side. Much redder than normal.	*Feb. 28, 1952.* No secretion. Redness gone.
37. B.DeS.	4	*Jan. 1953.* Muco-purulent secretion. M.M. red in R.M.B. Small ulcer?	*Feb. 25, 1953.* Muco-pus M.M. red R.M.B. Brg. - normal.	
38. V.P.	3	*Feb. 1944.* Frothy mucus both main bronchi. Redness and small ulcer R.M.B. at entrance to U.L.B.		
39. M.Z.	4	*Oct. 1951.* L.M.B. reddened mucous membrane. No obstruction or excess secretion.	*Mar. 1953.* Very little muco-purulent secretion. L.M.B. reddened. Minute ulcer. Brg. - normal.	
40. P.T.		*Mar. 14, 1950.* Larynx normal. Mucoid secretion both M.B. Mucous membrane much redder than normal.		
41. G.H.	11 mos.	*Jan. 1953.* Small amount viscid secretion. R.M.B. grossly swollen. Bleeding occurred readily.		

42. S.B.	4	*Feb. 1953*. Right Brg. normal. *June 1953*. Swollen mucosa L.M.B. *Right Brg.* normal.
43. D.P.	5	*June 1953*. Mucous membrane reddened at entrance to R.U.L. *R.Br.G.*-normal.
44. R.L.	6	*June 1953*. Carina thickened. L.M.B. filled with exudate. M.M. reddened throughout L.M.B. *Oct. 1953*. Some reddening bronchi L.L.L. *Br.G.* - normal.

During the 15 year period 144 children were examined bronchoscopically. Most of these had more than one such examination and many had bronchograms as well, so that altogether 273 bronchoscopic examinations and 118 bronchograms were carried out.

Practically all our work was done under general anesthesia administered by expert physician anesthetists. Ether and oxygen mixture was the commonest anesthetic agent. By means of this mixture the little patients were always kept well oxygenated and were in excellent condition at the end of the operation. Considering all the factors, this is the safest procedure at the present time in the opinion of our anesthesiologists. The use of general anesthesia allowed a careful, unhurried examination of the bronchial tree and eliminated any trauma from instrumentation. Small Jackson bronchoscopes were used and a Patterson forceps small enough to pass through a 3½ mm diameter bronchoscope was part of the equipment.

We feel that the meticulous checking of the lighting equipment by the bronchoscopist himself makes the procedure a safe one. Another safety measure is the special bronchoscopic room in which we work. This room is mechanically ventilated and humidified to prevent a concentration of the anesthetic. The table is shock-proof and all electrical connections and outlets are flash-proof. The use of woolen blankets in the operating room is prohibited.

The otolaryngological department does all the bronchograms for the chest service. These are carried out with the aid of the bronchoscope and follow the technique described in an earlier paper.[2]

The bronchoscope is passed under general anesthesia and as much of the secretions as possible are aspirated from the bronchial tree. One lung only is outlined at a time and the patient is put in the oblique position on that side. The opaque substance is then instilled through a long straight metal catheter through the bronchoscope. The radiologist who is watching the chest through the fluoroscope takes spot films at what he considers the right moment. For many years we have used Lipiodol,® and lately a Lipiodol-sulfanilamide mixture which alveolarized more slowly. We have tried other radiopaque substances but so far have not been able to obtain as good pictures with them.

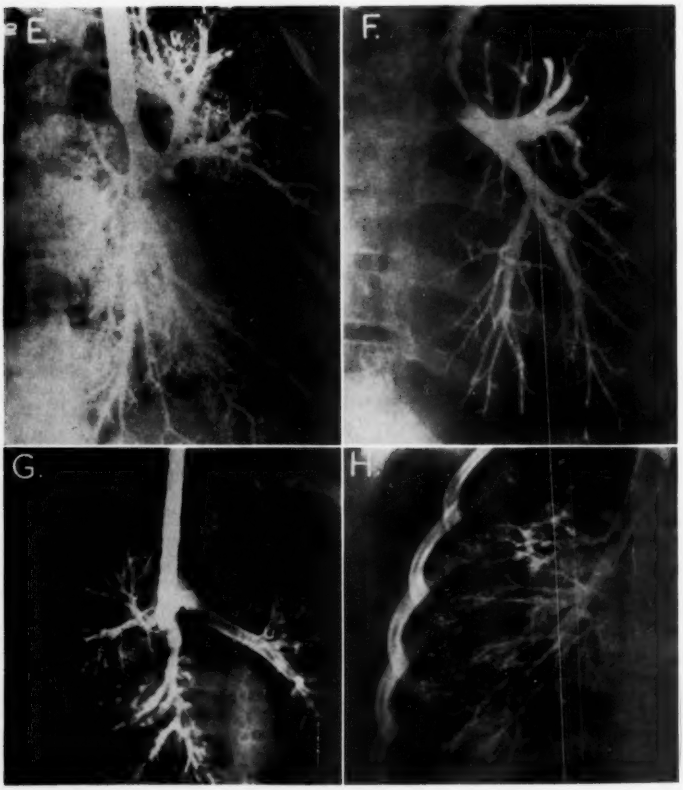

Fig. 2.—E. Complete obstruction of main stem of lingular bronchus 3 mm from its origin. F. Main stem left upper lobe bronchus unusually dilated as are the apical, posterior and anterior bronchus (bronchiectasis). G. Collapse of right middle and lower lobes. H. Marked bronchiectatic changes in the bronchus of the ant. segmental division of right upper lobe.

TABLE II

SECONDARY TUBERCULOUS BRONCHITIS AND BRONCHIECTASIS

CASE	AGE	BRONCHOSCOPIC FINDINGS			
1. J.W.	6	*May 1951.* L.M.B. clear. R.M.B. rounded bulge just below R.U.L.B. on antero-medial surface. Ulcerated on surface. Airway reduced ⅓ after suction to ½.	*Oct. 1951.* Little thin secretion all over. R.M.B. clear. Mucous membrane red right side.		
2. L.C.	3	*Dec. 1941.* Granulation R.M.B. Caseous in center. Hard caseous material consisting of caseous necrotic material and tubercle bac. aspirated.	*Mar. 1950.* Little thin secretion. Mucous membrane trachea and main bronchi very red.	*May 30, 1950.* Little thin secretion. Trachea and bronchi red. *R. Brg.* "Flagellata Bronchiectasis" R.L. & M.L.	*Sept. 5, 1950.* Some appearance. *Bronchogram* (rt). Upper normal Rt. main and lower lobe - proximal dil. "Flagellata bronchiectasis."
		Feb. 1952. Rt. lower lobe bronchus constricted. L. Bronchogr. - normal.	*Mar. 1952.* Right lower and middle lobe resected.		
3. J.M.	9 mos.	*Nov. 1951.* L.M.B. clear. R.M.B. full of caseous material. Removed by forceps - good airway after.	*Dec. 1951.* R.M.B. blocked with caseous material and granulation.	*Jan. 1952.* R.M.B. caseous material and muco-pus. Granulation entrance to lobe opposite R.U.L.B. - could not remove with forceps. Brg. - Bronchiectasis R.U. & M.L.	*Feb. 1952.* Resection R. U. & M. lobes.

4. D.P.	4	*Dec. 1949.* No obstruction. Mucous memb. l. side red and swollen. Rt. bronchial tree normal.	*June 1950.* Secretion ++. L.M.B. has granulation at entrance at orifice of U.L.B. Rest clear.	*Sept. 1950.* Pus from l.l.l. *Brg.* Bronchiectasis L.L.L. & Lingula.	*Nov. 1950.* Heavy purulent secretion l.l.l.
		Mar. 1951. Heavy pus l. side. Narrow constriction ½ way down l.m.b.	*May 1951.* Pneumonectomy (l).		
5. B.B.	12 mos.	*May 1953.* R.M.B. clear. L.M.B. obstructed by swelling from without lateral wall. Caseous material sucked out.	*June 1953.* Granulations removed left main bronchus. No bleeding.	*Sept. 15, 1953.* Asymptomatic. No obstruction nor granulations. Bronchus normal. Bronchogram normal.	
6. R.B.	5½	*May 1951.* Secretion rt. side. Large mass granulations entrance to R.U.L.B. Mass firm and could not all be removed.	*June 1951.* Muco-purulent secretion. R.M.B. clear. M.M. red but no granulations. Entrance inflamed. Possible granulation further in.	*Aug. 1951.* Muco-purulent secretion ++. Granulation R.U.L.B. Removed cleanly.	*June 1952.* Blood streaked ulcer R.U.L.B.
		Sept. 25, 1952. No ulcer. Brg. - bronchiectasis R.U.L.	*Nov. 1, 1952.* Brg. improved over June but still+.		
7. J.F.	3	*Mar. 1952.* Thin watery secretion. Brg. showed bronchiectasis R.M.L.	*Jan. 1953.* Mod. muco-pur. secretion rt. side granulations post. medial wall R.M.B. opposite U.L.B. *Brg.* Bronchiect. R.M.L.	Resection refused.	

TABLE II (Continued)

CASE	AGE	BRONCHOSCOPIC FINDINGS			
8. M.M.	2	*Mar. 1952.* Peanut removed. R.M.B. caseous material and granulations beyond this.	*Nov. 1952.* A little secretion of muco-pus. L.M.B. red and bled easily. *Brg.* Bronchiectasis R.U.L.		
9. M.K.		*Feb. 17, 1953.* M.L.B. clear. Orifice to basal division plugged with caseous granulation.	*Mar. 13, 1953.* Swelling L.M.B. Post-basal segment closed. Pus when granulation removed. Brgs. (l.) Complete obstruction to l.l.l. Rest of lung normal.	*May 28, 1953.* Gran. L.M.B. just below carina - medial side. Bled readily. L.L.L. bronchus still so stenosed no lipiodol went in.	*June 1953.* Small amt. of secretion. Granulation L.M.B. a little below carina on medial wall. Bled moderately.
		Sept. 15, 1953. Still impossible to get lipiodol into lobe. To be resected.			
10. E.F.	7	*Jan. 1951.* Tb granulations R.M.B. Ulcer beneath.			
11. D.T.	6½	*Oct. 1952.* Very little secretion. Red mucosa. Granulations removed R.M.B. - were tuberculous.			
12. L.Y.	9	*May 1951.* M.L.B. obscured by granulations, also basal segments. Bled easily. Adenomatous in appearance - were tb. granulations on section.	*June 1951.* Secretion +. Granular carina. Pus in R.M.L.B. R.M.B. clear but swollen.	*Nov. 1951.* Much secretion. Right side red. Granulations on carina. Rt. Brg. - Rt. lower lobe cronchiectasis.	*Dec. 1951.* L. Brg. normal. Resection rt. lower lobe.

13. J.W.	2	***Jan. 1950.*** **Tracheal mucosa red. Thin secretion both sides. R.M.B. compressed glands, ulcerated and bled easily.**	*July 1952.* Both main bronchi compressed to narrow chink by glands. Impossible to insert scope beyond.	*Oct. 1952.* Emergency suction because of collapse of l. lung by caseous granulation. Ulcer still + in R.M.B.	*June 1953.* No outside pressure. No evidence of disease. Rt. Brg. normal.
14. D.C.	15 mos.	*Apr. 1951.* Much secretion both sides - thin and clear. R.M.B. flattened from outside glands.	*May 1951.* Still reduced airway because of flattening from outside. Granular ulcer lateral wall.		
15. U.S.	10	*Mar. 1950.* Area of granulation L.M.B. about level of U.L.B. Sucked out, some blood.	*Sept. 1950.* Mod. thin secretion both M.B. Granulation to l. U.L.B. have gone. Mucous memb. of terminal part L.M.B. thickened, and granular.	*Nov. 1950.* L.M.B. clear. Slight secretion seen at entrance to terminal branch to ant. basal area. *Brg.* - l. lower and lingular disease.	*Apr. 1951.* Tiny granulation at edge of carina and at entrance to L.M.B. Rest clear.
16. L.C.	9	*Feb. 1950.* Bronchi healthy except R.M.B. which is ulcerated and full of granulations. Bled easily.	*Dec. 1950.* Trachea and L.M.B. healthy R.M.B. unchanged.	*May 1951.* Muco-purulent secretion +. No granulations . Inflamed area entrance to M.L.B. - still ulcerated.	
17. L.N.	9	*Feb. 1950.* Larynx and L.M.B. clear. Granulation antero-lateral side of R.M.B. opposite U.L.B. Thick bleeding material covers ulcer in this area.	*Mar. 1950.* Thin secretion +. Granulation R.M.B. medial side. Ulcer edge of carina. Remainder normal.	*May 1950.* Granulations at entrance to R.U.L. bronchus - did not bleed.	*Oct. 1950.* Tiny granulation just below carina at R.M.B. Less than before.
		Nov. 1950. Tiny granulation medial wall R.M.B. No red. Did not bleed. Brg. (r) Neg.	*May 1951.* Small granulation entrance to R.U.L.B. Mostly removed by forceps.	*June 1951.* Mucous membrane R.M.B. red. No obstruction. No granulation.	

TABLE II (Continued)

CASE	AGE	BRONCHOSCOPIC FINDINGS			
18. A.A.	2	*Feb. 1950.* R.M.B. obstructed just below carina by masses of caseous material and granulations. Removed as much as possible.	*Mar. 1950.* R.M.B. ulcerated - bled freely.	*Sept. 1950.* Bloody granulations blocking terminal div. of R.M.B. Brg. shows R.M. & L.L. collapse. Portion of this area cystic or contains cavities.	*Mar. 1951.* Resection Rt. middle and lower lobe.
19. P.S.	7	*Mar. 1952.* Very little bloody secretion. Large caseous granulations in lower trachea and entrance to R.M.B.	*Apr. 1952.* Heavy secretion in trachea. Large granulations at entrance to R.M.B. Removed with difficulty. Some still left.	*May 1952.* Granulations on rt. wall of trachea above carina. Ulceration R.M.B.	*July 1952.* Large granulation rt. wall of trachea and R.M.B. Partially removed.
		Oct. 1952. Large granulation entrance R.M.B. Removed as well as possible. *Rt. Brg.* - normal.			
20. M.S.	2	*Nov. 1952.* Large gland pressing on rt. bronchus. Thickening of mm. Mucopus.	*June 1953.* Fair amount of blood stained mucopus. *R. Brg.* Bronchiectasis Rt. U. Lobe.		
21. J.S.	13	*Jan. 1952.* Large amount mucopus coughed out and more sucked out. M.M. dull red throughout. Brg. upper lobe bronchiectasis with prox. dil. and peripheral tapering.			

22. J.C.	2	*Nov. 1952.* Heavy mucopus l. side. *L. Brg.* - no abnormalities.	*June 1953.* Very little secretion on all l. side. *Rt. Brg.* - normal.		
23. L.S.	6	*Jan. 1950.* Tracheal mucosa red. Thin secretion both sides. R.M.B. red and ulcerated. Granulation entrance to R.U.L.	*Apr. 1950.* Bronchi clear. No abnormality.	*May 1951.* Larynx and trachea red, also carina R.M.B. small bleeding ulcer. *R. Brg.* - normal.	*Sept. 1951.* Secretion and redness l. side. L. Brg. Bronchiectasis L.L.L. and lingula.
24. R.A.L.	10	*Jan. 1952.* Moderate amount of mucopus aberrant bronchus R.U.L. from lateral wall of trachea. Caseous granulations R.M.B. Brg. Rt. - bronchiectasis R.U.L. dorsal and basic branches R.L.L.	*Feb. 1952.* L. Bronchogram normal.	*Mar. 1952.* Rt. M. & L.L. resected and later anomalous R.U.L.	
25. G.H.	14	*Feb. 1953.* Much thin secretion coughed out. R.M.B. inflamed, small granulation just inside the orifice.	*June 1953.* Small amount white secretion. Mucosa healthy. *Brg.* - R.U.L. bronchiectasis.	*Sept. 15, 1953.* Small amount of secretion but no other abnormality. *Brg.* - normal.	
26. M.M.	9	*June 1952.* Slight secretion. Mucous memb. red R. side. Extensive swelling R.M.B. No ulcer nor granulation.			
27. D.T.	6½	*Oct. 1952.* Very little secretion. Red mucosa rt. side. Granulation R.U.L.B. removed.			

TABLE II (Continued)

CASE	AGE	BRONCHOSCOPIC FINDINGS			
28. L.W.	4	*Dec. 1943.* Collapsed L.U. L. Bronchi constricted. Little mucoid secretion. Granulation L.M.B.	*May 1944.* Muco-purulent secretion. No granulations. *Brg.* - Collapse of bronchi L.U.L. but no ectasia.		
29. R.Z.	3	*Aug. 1951.* Large tuberculous granulations blocking R.M.B. Removed by forceps.	*Feb. 1952.* Blood secretion Granulation R.U.L. bronchus - bled freely. Brg. (rt.) - bronchiectasis R.M. & L. lobes.		
30. R.L.	5	*June 1953.* Much whitish discharge l. side. Rt. main bronchus constricted - could not pass 'scope.			
31. J.W.	2	*May 1952.* Some thin secretion. A little reddening of mucous membrane of main bronchi.	*July 1952.* Carina and entrance to both main bronchi markedly compressed from anterior aspect.	*Mar. 1953.* Small granulation in left main bronchus just at carina on medial wall. *R.Br.G.* - normal.	*May 1953.* A little reddening of mucous membrane. *Rt.Br.G.* - normal. cepscre-wall.
32. D.F.	9	*Oct. 1953.* Moderate amt. mucopus. Granulations seen in R.U.L.B. *Rt. Brg.* Poor filling of R.U.L. particularly out apical segment.	*Mar. 1954.* Granulations in R.U.L.B.	*Apr. 1954.* No granulations in R.U.L.B. *Rt.Br.G.* R.U. lobe filled well.	

33. M.K.	4	*Feb. 1953.* Orifice of left post. basal bronchus occluded with granulations. *Feb. 1953.* Swelling and granulations around orifice l.l. lat. and post. basal bronchi. Pus coming from l.l. basal. No F.B.	*March 1953. L.Brg.* - No lipiodol in bronchi of l.lobe. Complete obstruction. *March 1953.* Much swelling in L.M.B. in region of orifice of basal segments. Pus escaped after spreading with forceps.	*May 1953. L.Br.G.* No lipiodol in L.L.L.B. Lower left lobe alilectatic with stenosis of bronchi.	*Sept. 1953. L.Br.G.* Poor entry into left side. *Nov. 1953.* L.L.L. lobectomy.
34. M.B.	5	*Oct. 1953.* Large granulation removed from L.M.B. *L.Br.G.* - some blunting & irregularity of terminal bronchi.			
35. S.P.	3	*Nov. 1953.* Fairly large amount bloodstained mucopus. *L.Br.G.* L.L. lobe completely collapsed.	*April 1954.* Collapse and bronchiectasis of L.L.L.	*Mar. 1954.* L. lower lobectomy.	
36. J.W.	20 mos.	*June 1951.* A little thin secretion. Bronchi healthy.	*May 1952.* L.Br.G. - normal (stricture missed).	*Nov. 1952. R.Br.G.* - normal.	*Nov. 1953. L.Br.G.* - constriction of apical post branch of L.U.L.B. *Dec. 1953.* Lobectomy left upper lobe.
37. G.H.	14	*Feb. 1953.* R.U.L.B. inflamed. Small granulation in this bronchus.	*Mar. 1953. R.Br.G.* - Apical branch of R.U.L.B. shows some thickening and dilation due to bronchiectasis.	*Sept. 1953. L.Br.G.* Normal.	*Dec. 1953.* M.M. thickened at carina. *R.Br.G.* - apical branch of R.U.L.B. shows signs of bronchiectasis. *Jan. 1954.* Lobectomy - right upper lobe.

TABLE II (Continued)

CASE	AGE	BRONCHOSCOPIC FINDINGS			
38. P.I.	8	*Dec. 1953. Br.G.* - R. - varying degrees of cylindrical and saccular bronchiectasis involving lower lobe.	*Feb. 1954.* R.L.L. lobectomy.		
39. M.M.	2 (twin)	*Mar. 1954.* M.M. reddened throughout. Few small bleeding granulations in R.U.L.B.			
40. L.D.	12 mos.	*Aug. 1954.* R.M.B. - completely just beyond carina with granulations. Granulations removed.	*Sept. 1954.* R.M.B. - blocked with granulations. Removed. Edemations m.m. beyond this.	*Nov. 1954.* No granulation seen. *Br.G.* - R. - normal.	
41. R.B.	2	M.M. very red. Br.G. R. - Upper lobe bronchus showed delay at filling. Apical branch dilated.			
42. F.D.	5	*Oct. 1954.* Granulation in R.M.B. at entrance to R.M.L.B. obstructing. Removed. *Br.G.* - R. no filling of mid lobe and collapse of lower lobe.	*Mar. 1955.* Br.G. - R. - Middle lobe & lower lobe filled well.	*Sept. 1957.* Br.G. R. - Normal.	*Nov. 1957.* Br.G. L. - Normal.

43. N.B.	16 mos.	**_Oct. 1954._ R.M.B. almost completely blocked with granulations. Removed. _Br.G.-R._ Collapse middle & lower lobes.**	*Apr. 1955.* Grans. in R.M.B. just beyond carina. *Br.G.-R.* R.M.L. bronchiectasis and collapse lower lobe.		
44. T.T.	12 mos.	**_Oct. 1954._ L.M.B. reddened. Fine granulation at entrance to L.U.L.B. _Br.G.-L._ non-filling of apical posterior segment L.U.L.B.**			
45. L.M.	18 mos.	**_Nov. 1954._ Grans. in R.U.L.B.. Removed. _Br.G. R._ - Minimal narrowing R.U.L.B. Good filling of all bronchi.**			
46. L.P.	6 mos.	**_Nov. 1954._ Mass granulations in R.M.B. Caseation**	in grans. *Nov. 1954.* Mass grans. in R.M.B. again. Removed.	*Dec. 1954.* Grans. in R.M.B. attached to arteromedial wall. Removed.	*Apr. 1955.* M.M. reddened. No granulations. *Br.G.-R.* normal.
47. P.L.	8	**_Apr. 1955._ _Br.G.-L._ Bronchiectasisi n apical post. Segment of L.U.L.B.**	*May 1955.* L.U.L. lobectomy.		
48. R.H.	6	**_May 1955._ Large granulations in R.M.B. at R.U.L.B. Removed.**	*Nov. 1955.* Granulationsi in R.M.B. at R.U.L.B. *Br.G.-R.* - Filling defect in R.U.L.B.	*Jan. 1956.* R.U.L. lobectomy.	
49. A.M.	3	**_May 1955._ L.M.B. occluded by granulations. Removed.**	*July 1955.* L.M.B. almost occluded by grans. Removed.	*Oct. 1955.* Both main bronchi clear. Openings of accessory bronchi well seen.	

TABLE II (Continued)

CASE	AGE	BRONCHOSCOPIC FINDINGS			
50.	16	***June 1955.* Br.G.-L. Main stem of lingular bronchus of L.U.L.B. completely occluded at 3 mm from origin.**	*Oct. 1955.* Br.G.-L. - Lingular bronchus could not be filled.	*Jan. 1956:* Lingulectomy.	
51. R.P.	8	*Nov. 1955.* Pusi n L.M.B. *Br.G.* - L. - Poor filling of lingular bronchus.	*Mar. 1956.* Small gran. at entrance to L.U.L.B. Removed. *Br.G.-L.* - Poor filling of lingular bronchus. Some degree of bronchostenosis.	*Apr. 1956.* Lingular bronchus open. M.M. reddened.	*Aug. 1956.* Lingulectomy L.L. lobectomy.
52. D.J.	2	*Nov. 1955.* R.M.B. filled with granulations and caseous material. Removed. Br.G.-R. - Atelectasis and bronchiectasis of lower and middle lobes.	*Feb. 1956.* R. Mid. and lower lobectomies.		
53. D.M.	14 mos.	*Dec. 1955.* L.M.B. occluded by granulations. Large granulation in R.M.B. not obstructing. Grans. removed.	*Mar. 1956.* Both main bronchi clear. No grans.		
54. K.M.	6	*Oct. 1955.* Swelling under post mucosa at orifice of R.U.L.B. Biopsy.	*Oct. 1955.* Exploratory thoracotomy - gland biopsy. T.B.	*Apr. 1956.* *Br.G.*-R. - Bronchial stump of R.U.L.B. terminates abruptly 4 mm from R.M.B.	

55. L.H.	6	*July 1956*. Polypoid granulations from R.M.L.B. orifice. Removed.	*Aug. 1956*. Small gran. in R.M.B. at opening of R.M.L.B. Removed.		
56. M.M.	14	*Aug. 1956*. Inflamed area of m.m. at entrance to L.U.L.B.	*Mar. 1957*. Br.G.-L. - Central bronchiectasis of L.U.L.B. and apical, post., and lingular branches.		
57. L.B.	4	*Aug. 1956*. Granulation at entrance to R.U.L.B. Removed.	*Nov. 1956*. Granulation at entrance to R.U.L.B. Removed.	*Jan. 1957*. Granulation at entrance to R.U.L.B. Removed. *Br.G.-R.* - Bronchiectasis of post. segmental bronchi of R.U.L.B.	*Mar. 1957*. Thoracotomy - R.U. Lobectomy postponed because of many adhesions.
58. A.L.	2	*Aug. 1956*. Emergency bronchoscopy. Large mass of granulations at entrance to R.M.B. Occluding it. Removed.	*Nov. 1956*. Both main bronchi clear.		
59. J.D.	6 mos.	*Dec. 1956*. R.M.B. occluded by granulations and caseous material. Removed.	*Jan. 1957*. Large gran. in upper part R.M.B. just below opening of R.M.L.B. Removed.	*June 1957*. No granulations. *Br.G.-R.* - Normal.	
60. P.W.	10	*Dec. 1956*. Purulent secretion. Granulations and caseous material on right side of carina. Removed.	*Mar. 1957*. Granulation removed from edge of carina.		

TABLE II (Continued)

CASE	AGE	BRONCHOSCOPIC FINDINGS		
61. M.P.	5	*Apr. 1957.* Granulation and caseous material in R.M.B. just above entrance to R.M.L.B. Removed.	Much bloody mucopus aspirated from below this.	*May 1957.* Swelling of m.m. of R.M.B. at orifice of R.M.L.B. Caseous material in center of this. Removed. Fair amount of mucopus.
62. L.S.	8	*June 1957.* Br.G.-R. - Marked bronchiectasis in art. segmented branches of R.U.L.B.	*Nov. 1957.* R.U. Lobectomy.	

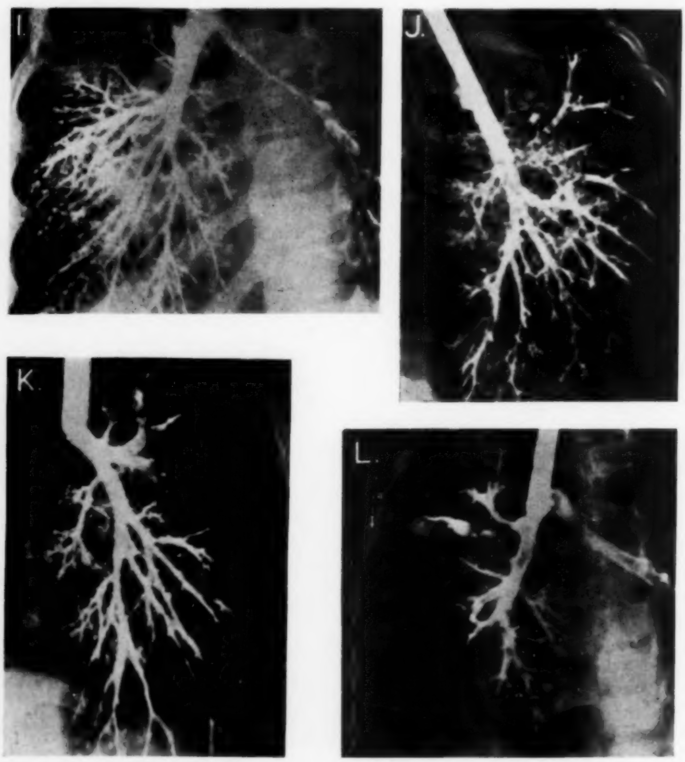

Fig. 3.—I. Complete occlusion of right upper lobe bronchus at 4 mm from its origin. J. Non-filling of the apical posterior segment of left upper lobe bronchus. K. Lingular bronchus not well filled. Some degree of bronchial stenosis. L. Gross deformity of posterior segmental bronchus of right upper bronchus (bronchiectasis).

Bronchograms have been done infrequently by some workers in this field because they considered the procedure somewhat dangerous.[3] We have found it perfectly safe and easy to do when using the bronchoscope technique and have carried out the procedure as often as we were asked to do so.

At the commencement of this work 25 cases of tuberculosis without endobronchial disease were examined bronchoscopically to look for a source of persistent positive sputum, and to determine a norm. Eight bronchograms with normal results were also carried out. These cases are not recorded in the table at the end of the paper, as it is simpler to describe them here. Little or no secretion was found, and whn present was of a mucoid type. The bronchial mucosa was reddened but in a generalized manner, showing no localized lesions.

Endobronchial tuberculosis is of two types, primary and secondary. The primary type has been said to be of rare occurrence in children[4] but we found it frequently in our series. It is the result of a direct infection of the bronchial mucosa by the implantation on its surface of infected material, or by the hematogenous and lymphatic routes. The bronchoscope revealed redness and swelling of the mucosa localized to a segment. The commonest areas affected were the bronchi of the upper lobes, the right middle lobe, and occasionally the lingula. The bronchi sometimes appear shrunken and collapsed. On the other hand, bronchoscopic examination may reveal no change, but the bronchogram will show the results of the disease. Shrunken lobes are common.

Secondary tuberculous bronchitis is a much more dramatic type of infection, and may at times call for emergency bronchoscopic treatment to relieve obstruction. The disease in these cases originates exobronchially.

Examination may reveal compression of a bronchus from extraneous glands or a further progression of this localized disease. The gland may have ruptured through the bronchial wall producing ulceration, masses of caseous material or sessile granulations. The effect may be similar to a foreign body, particularly when it comes on suddenly and emergency bronchoscopy may be necessary to remove the obstruction. On the other hand, the granulations may be smaller but gradually grow to plug a bronchus. Pieces of granulation tissue,

TABLE III

CASE WHICH DID NOT SHOW ENDOBRONCHIAL DISEASE ON BRONCHOSCOPIC EXAMINATION

(IN ADDITION TO THE ORIGINAL 25 CASES)

CASE	AGE	BRONCHOSCOPIC FINDINGS		
1. B.B.	9	*Oct. 1953. R.Br.G.* - Normal.		
2. M.R.	3	*May 1953.* Excess yellowish secretions. *Dec. 1953.* A little mucopus. *Br.G.Rt.* - Normal.		
3. M.M. (twin)	2	*Mar. 1954.* - Normal bronchi.		
4. L.C.	5	*Apr. 1954.* - Br.G.-L. - Atelectasis L.L.L.	*Oct. 1954.* Atelectasis L.L.L.	*May 1955.* Br.G.-R. - Normal.
5. L.T.	9	*Oct. 1954.* Br.G.-L. - Normal.		
6. C.T.	20 mos.	*May 1955.* Br.G. - Normal.		

7. G.C.	5	*Dec. 1955.* Much heavy secretion of mucopus from both lungs. M.M. of bronchi reddened.	*Nov. 1956.* Br.G.-L. - Bronchiectasis of ant. basic division of L.L.L.B. Lingula did not completely fill.
8. H.W.	2	*Dec. 1955.* Thin mucopus from each main bronchus. M.M. reddened throughout.	
9. P.O.	7	*Nov. 1956.* Whitish secretion. M.M. reddened throughout.	
10. L.G.	11	*June 1957.* Br.G.-R. - Bronchi of lower lobe are crowded together and do not fill well. Marked pleural thickening in this area.	*Sept. 1957.* Decortication of right pleural space with excision of loculated empyema.
11. E.Z.	4	*Sept. 1957.* Br.G.-R. - Normal.	
12. C.S.	5 mos.	*Nov. 1957.* Reddening of m.m. of bronchi.	
13. L.F.	3	*Nov. 1957.* Much mucoid secretion. Main bronchi normal.	

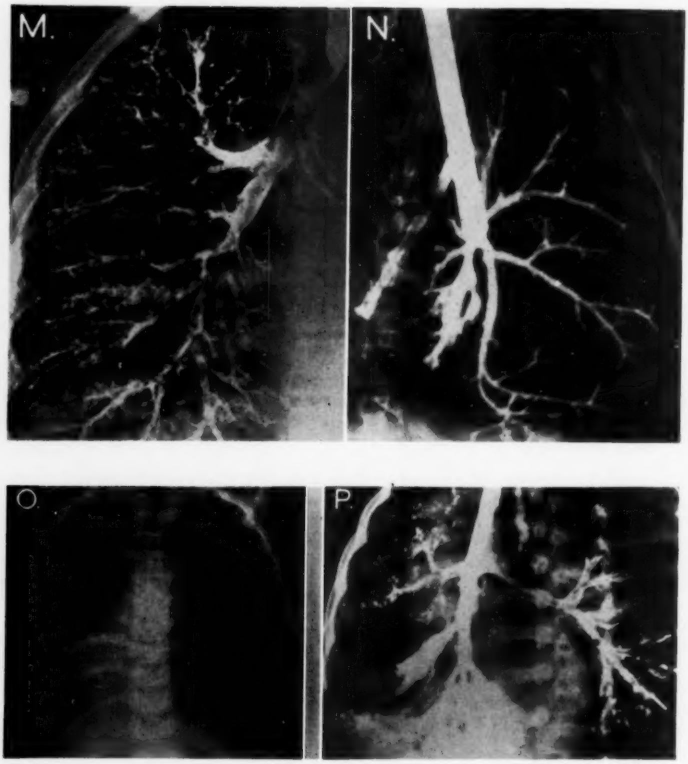

Fig. 4.—M. Bronchiectasis of apical branch of right upper lobe bronchus. N. Collapse and bronchiectasis of left lower lobe. Note lingular branch making a right-angled curve at diaphragm. O. A.P., chest plate showing collapse right lower lung field. P. (Same case as O) Atelectasis and bronchiectasis of right middle and lower lobes. Upper lobe has expanded to fill rest of hemi-thorax.

or caseous material, may break off and plug a lower bronchus or even a bronchus in the other lung. This type of disease may involve any part of the bronchial tree, but is commonest in the lower lobes, and then the middle lobe or lingula.

The signs and symptoms of tuberculous bronchitis are generally more marked in the secondary type. A wheeze is frequently present leading to a diagnosis of asthma or a foreign body. The true etiology may not be discovered until the bronchoscopic examination is carried out revealing tuberculous granulations.

An overdistended lobe is often produced in secondary endobronchial tuberculosis and the ectatic changes as revealed in the bronchogram are characteristic. The proximal bronchi are dilated and their distal portions normal or narrowed, the so-called "flagellate" bronchiectasis. There is peripheral alveolarization like a normal lung as opposed to the shrunken lobe of the primary type. On the other hand, the bronchiectatic changes may be the same as those due to any long-standing obstruction and infection.

During the passing of the bronchoscope in these cases the condition of the larynx and trachea was always noted. Only twice was ulceration seen on a vocal cord. To us it seemed that this type of tuberculosis was rare in children. Occasionally, some thickening of the carina was noted but tracheal stenosis was not seen.

There have been considerable advances in the treatment of endobronchial tuberculosis in the last few years. This is due mainly to two factors, drug therapy and mechanical interference.

The chief drugs used are streptomycin, para-amino salycylic acid (PAS) and isonicotinic acid hydrozide (INH). Streptomycin was the first drug of this group to be used, but the results were not up to the hopeful expectations. The failure of this drug therapy was probably the inability of streptomycin to destroy intracellular organisms, or to penetrate the caseous masses. I.N.H. possesses both these properties and looks like a more successful drug to use. When surgery is contemplated streptomycin is given pre-operatively along with I.N.H. Also, if a patient does not seem to be doing well enough on I.N.H., the addition of P.A.S. sometimes gives better results.

Mechanical interference includes bronchoscopy and excisional therapy such as lobectomy or occasionally pneumonectomy. Repeated bronchoscopic aspiration of secretions and removal of obstructing material together with the administration of I.N.H. has had gratifying results in our cases. A bronchoscopic examination may reveal much granulation tissue plugging a bronchus. This is removed as well as possible and the patient put on or kept on the drug. Another examination in a short while may reveal the granulations to be fewer in amount and they are again removed. This is noted on further examinations until the granulation tissue has completely disappeared. Sometimes on the second bronchoscopic examination it is seen that there has not been a recurrence of the granulations. These results have been recorded in the tables at the end of the paper.

Those patients who have well established bronchiectasis when first seen are not going to be helped greatly by either drugs or bronchoscopy and early surgical excision is indicated.[5]

SUMMARY

The bronchoscopic findings in 144 children with pulmonary tuberlulosis are reported.

The difference in the two types of endobronchial tuberculosis is noted.

Treatment is discussed from the point of view of drug therapy and mechanical interference.

170 St. George St.

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LV

THE CLINICAL SIGNIFICANCE OF THE ANATOMICAL ARRANGEMENT OF THE PARANASAL SINUSES

FRED W. DIXON, M.D.

CLEVELAND, OHIO

This subject is of interest to the rhinologist in interpreting the symptoms of sinusitis and on surgical intervention to appreciate their variations.

In an examination of over 200 wet specimens, the sinus arrangement in no two were exactly the same, in fact the two sides were rarely symmetrical. The sinuses most constant in shape and size were the maxillary. The least predictable were the sphenoids. The frontals and sphenoids frequently crossed the midline, while the ethmoids never invaded beyond the midline.

The maxillary sinus was always present. While the capacity may reach 20 cc, the average capacity was 15 cc. In one specimen the capacity was 1 cc in an otherwise normal skull. This, as well as the narrow width frequently encountered, makes irrigation a procedure to be done with caution. One maxillary sinus was double; each with a common ostium in communication with the ethmoidal infundibulum. Another had a midline partition almost completely dividing it into an anterior and posterior compartment. Six pea-sized pockets having no relation to the tooth sockets were noted on the floor of another which would favor retention of secretion on irrigation and would be confusing in the roentgenogram.

The natural ostium was accessible in approximately 30% of the specimens, 10% more had one or more accessory ostia in the middle meatus, while in 25% the membranous wall in the middle meatus was so transparently thin that it could be punctured easily by a semi-sharp instrument. This would be in agreement with most

rhinologists that approximately two-thirds of the maxillary sinuses can be irrigated through the middle meatus either by an ostium or by puncture. Transillumination gives a clue as to the density of the bony wall of the opposite maxillary sinus. If the wall is thin and there is no history of previous infection, then either the middle or inferior meatus can be punctured painlessly. The approach through the inferior meatus is more trustworthy and like a puncture through the middle meatus, leaves the ostium free for the return flow. A notation made on the patient's chart will be of value should an infection return later. Transillumination, while informative, is no substitute for a good roentgenogram. There is no substitute for a careful examination.

The frontal sinus, rarely a simple, smooth chamber, battles for position with its fellow on the opposite side and with the ethmoid on the same side. The terminology of these cells varies according to the anatomist as ethmoid, ethmofrontal, frontal recess, accessory frontals, or double frontals, depending on whether they are being classified genetically or topographically. The essential problem is to secure drainage and ventilation. Four per cent of the skulls showed no invasion of the frontal sinus into the perpendicular plate, but in these skulls the frontal sinus may develop into the horizontal plate. Ten per cent had only one frontal which invaginated a large portion of the perpendicular plate, while its fellow on the opposite side had never gone beyond the roof of the nasal cavity. In one wet specimen the two frontals communicated by an ostium; while in another, two openings were seen. Bullar cells ware found in 8% of the specimens, usually on the posterior wall. These have no connection with the frontal sinus, but are ethmoid cells which have grown into the frontal cavity.

The horizontal plate, or orbital plate, of the frontal bone, was completely invaded by frontal or ethmoid cells in 5% of the specimens. In some instances the frontal and the sphenoid sinuses had a common wall. Compartments and multiple cells in this bone will be confusing to the surgeon and difficult to delineate by roentgenogram. However, these cells always open from their genetic origin so that when the ethmoid labyrinth is opened, either externally or intranasally, proper drainage should be afforded.

The ethmoid sinuses contain from two to twenty cells of many shapes and sizes and, like boys rushing for seats at a baseball game,

strive to get there "first with the mostest." Due to their early development, they pneumatize surrounding structures, but are in turn rarely invaded. While the anterior ethmoid cells drain into the middle meatus and the posterior ethmoid cells drain into the superior and supreme meatus, the sinuses themselves may be superior, inferior, internal or external to each other. While it is interesting to classify these cells anatomically, the surgeon is primarily concerned with the landmarks and the intelligent appreciation that these cells may be found in many locations.

The middle turbinate was invaded in 17% of specimens by cells from one or both of the anterior or posterior group. It has been my custom to view with suspicion a large middle turbinate in a person with headache. This may interfere with sinus drainage or be the seat of an empyema. In two specimens the maxilla was invaded by a posterior ethmoid cell which had driven down and behind the maxillary sinus, but drained into the superior meatus.

The optic nerve was seen prominently in 4% of specimens in a posterior ethmoid cell; while in 8% of the specimens the optic nerve indented the sphenoid sinus.

In an examination of several hundred wet specimens, the sphenoid sinus was never absent. In some instances the sinus was mostly membranous and produced so small a dimple on the bony surface that it could readily pass unnoticed when the mucous membrane was removed. The cancellous bone was invaded by either sphenoid sinus which resulted in every conceivable shape. They may be superior, inferior, internal or external to each other. They may also completely surround their opposite fellow so that the important structures on both sides indent only one sinus. They may invade the greater and lesser wings of the sphenoid and pneumatize the pterygoid process. The capacity varied from 0.1 cc to 14 cc on each side, with an average of 5 cc.

The sphenoid, occupying as it does, the central portion of the skull, and being in close proximity to the internal carotid artery, the vidian, the optic and the maxillary nerves, and those important structures within the cavernous sinus, can easily be the most dangerous sinus to subject to surgery. Septa were seen in 22%. These usually arose from the posterior inferior wall and were so large and so placed

that inspection of the sinus would be impossible at operation. Surgical removal of these partitions may result in osteomyelitis and a spread of infection. Dehiscences in the septal wall of the macerated specimens were seen five times in 1,600 skulls. I did not observe any dehiscences in the membranous wall of the wet specimens examined, but believe the infection could easily travel along the arteries which pierce the walls. Infections resulting in the thickened bone and diseased membrane have, however, been observed in the sphenoid while the ethmoid cell, separated by a thin, bony partition, showed no infection.

The pterygoid canal was so prominent in 7% of the specimens that any surgery would have resulted in injury to the vidian nerve.

In an examination of 1,600 macerated skulls, the distance in mm from the anterior nasal spine to the sphenoid ostium was as follows:

	ANTERIOR NASAL SPINE TO OSTIUM		ANTERIOR NASAL SPINE TO PITUITARY FOSSA	
1600 Skulls	White	Negro	White	Negro
263 Female	56.71	57.64	70.20	71.49
1337 Male	60.93	60.60	75.67	75.28

(In office practice and nonmacerated skulls 10 mm should be added to these measurements).

Thus it is seen that the average distance from the anterior nasal spine to the sphenoid ostium and to the anterior surface of the pituitary fossa depends not on race, but on sex. The ostium may be either round or oval, the proportion being two to one in favor of the round opening. In an examination of 1,600 macerated skulls previously reported, the diameter when round was 5.03 mm, when oval 4.2 mm by 5.8 mm. Before maceration the mucous membrane covering the edge of the bony ostium was usually 1 mm in thickness, thus reducing the membranous opening by 2 mm. The distance from the cribriform plate to the center of the bony ostium varied from one to 15 mm, the average being 8.25 mm. The average distance from the septum to the center of the ostium was 4.92 mm. The exception to this was found when a large posterior ethmoid cell had

developed superior to the sphenoid. In this event the ostium was approximately 2.4 mm from the angle formed by the cribriform plate and the septum.

The anterior wall of the sphenoid usually slopes down and backward in which event the ostium faces forward. In some instances the anterior wall slopes back superiorly in which the ostium points upward. Occasionally the ostium pointed outward and in others inward. In these locations catheterization would be impossible.

Successful catheterization of the sphenoid ostium will be partly dependent upon the angle formed by the turbinates and the septum. When the septum is deflected or the turbinates large, manipulation of the catheter will be hampered. When the angle is less than thirty degrees, catheterization is usually impossible. This space, rather than the size of the ethmosphenoidal recess is the determining factor. Various authors have reported catheterization in office practice varying 60% to 90%. Success will depend upon the location of the ostium, its size, the plane of the anterior wall, and the patience of the operator.

The fovea ethmoidalis posteriorly is usually twice the width of the anterior portion. It can be cleaned thoroughly by tilting the head. If the surgeon preferring the intranasal approach will preserve this landmark, the orbital plate externally, the curtain of mucous membrane covering the superior and supreme turbinates, and as much as possible of the mucosa covering the middle turbinates, he will be on safe ground. In 35 years of following this technique I have had no serious complications.

When a single polyp occurs in the nose it can be removed without extensive surgery, but where multiple polyps are found, thorough removal will give the most satisfactory results. A deflected septum which interferes with visualization of the operative field should be corrected at the same time. After removal of the ethmoid cells, the sphenoid ostium is examined. If no pus is seen coming from the sphenoid sinus and a cotton applicator placed into the sinus returns unsoiled, the sinus is not disturbed. Frequently an infection involving the remaining sinuses will subside after the ethmoid labyrinth has been unblocked. An infected maxillary sinus may respond to irrigation when free drainage has been established. The sense of smell has returned in some patients after an absence of eight years.

While crusting has been observed in some patients; especially following a cold, it has not been a common complaint. Dryness of the throat will not result if the curtain of mucous membrane previously described is preserved. Polyps may recur, especially in the allergic individual. The most satisfactory results will be obtained by thorough removal and control of the allergy. The poorest results follow partial removal. In a previous report of 200 ethmoidectomy operations, followed on an average of ten years, 75% had no recurrence, 25% recurred mostly in the allergic individuals or where the physical condition of the patient did not allow a complete removal. Sections of mucosa taken from the operated area of the fovea ethmoidalis one year later showed "the mucous membrane was covered with pseudostratified columnar epithelium. In some areas cilia were identified. There was an increased number of enlarged cells containing vacuoles, namely, goblet cells containing mucin. The nuclei were vesicular and contained an average amount of chromatin material. The basement membrane was somewhat thickened and had a deep pink appearance. The underlying tissue contained many blood vessels and in addition there were glands, predominantly of the mucous type."

CONCLUSION

Variations in the shape, size and arrangement of the nasal accessory sinuses have been described. While cellular arrangements may vary, certain boundaries remain constant which, if known and observed, will render sinus surgery satisfying to the patient and to the surgeon.

1027 Rose Bldg.

LVI

ORBITAL APEX SYNDROME

Austin T. Smith, M.D.

Philadelphia, Pa.

The orbital apex syndrome is the name applied to the clinical manifestation of a lesion which affects the nerves and vessels that pass through the optic foramen and the sphenoid fissure. The characteristic symptoms are: impairment or loss of vision, ptosis, diplopia and pain. The pain is usually severe, and located in the temperoparietal region. The etiology of the lesion may be infection, neoplasm or trauma and it may originate in the retro-orbital region or in the nasal sinuses, particularly the posterior group. This symptom complex which may appear with dramatic suddenness is usually a warning of serious disease and when encountered by internists, ophthalmologists, neurologists or otolaryngologists, the best co-operative efforts of all are necessary to establish its pathogenesis and the best plan of treatment.

The purpose of this discussion is to emphasize the importance of the orbital apex syndrome as a manifestation of sinus disease. These observations are based upon my experience with five patients in which it was the most prominent, and in some the only clinical evidence of pathology in the sinuses.

Orbital complications from sinus disease are not unusual, and have been described and classified by many observers.[1] The most familiar are those due to invasion by an infectious process which destroys the thin osseous partition separating the sinus from the orbit or to invasion by lymphatic and venous channels. They were much more common prior to the use of antibiotics and chemotherapy when rapidly spreading virulent infection frequently caused multiple sinus involvement, and the orbital wall was penetrated at many points. The frontal and ethmoid sinuses are the usual primary sites. Antibiotic and chemotherapy, which are now used empirically in the treatment of all types of sinus disease, may prevent the spread of

virulent infection to the orbit, but pyoceles or mucoceles which are the sequel of unresolved sinus inflammation can still erode the thin osseous barrier and penetrate the orbital cavity. Neoplasms of the sinuses act in a similar manner. Frequently the orbital complications are the only evidence of such sinus lesions. The characteristic symptoms of orbital complications due to this type of lesion are diplopia and visual disturbance from pressure of a space taking mass which causes displacement of the bulb and impairment of function. There is an absence of the inflammatory reaction seen in those due to acute virulent infection. The peri-orbita is tough and it is not easily penetrated.

The orbital apex syndrome when it is caused by sinus disease, differs from the orbital complications enumerated, in that there is an absence of inflammatory reaction, and also little or no displacement of the bulb. The bulb is fixed in the straight ahead position due to paralysis of the III, IV, and VI nerve, whereas in the other complications the position of the bulb is determined by infiltration or compression by the lesion. Tenderness is slight or absent, but pain behind the eye and in the temperoparietal region is prominent and often severe, due to involvement of the ophthalmic branch of the V nerve. The structures are affected as they enter the apex, rather than by direct invasion of the orbital walls, and the sinus pathology most frequently found is in the posterior ethmoid or sphenoid sinuses. However, upon an anatomical basis it is possible for a lesion of the maxillary sinus to be the primary factor.

The observations which I wish to make on this syndrome are really elementary in the light of our present knowledge of the anatomic, histologic and physiologic characteristics peculiar to the sphenoid and ethmoid sinuses. The importance of these characteristics in the pathogenesis of disease has been recorded by a long list of distinguished investigators from the early years of our specialty to the present time. The names of Proetz,[2] Van Alyea[3] and Schaeffer[4] stand out as contributors to this knowledge. The clinical significance of the anatomic characteristics of the sinuses as the basis of this syndrome is shown in Table I.

Each of the five patients that are the basis for this discussion presents a clinical problem in diagnosis and treatment of sufficient interest to warrant giving a detailed case report. However, this

would be too time-consuming, tedious and repetitious for this presentation. I shall only cite briefly therefore extracts from each clinical history to illustrate how different types of sinus lesions such as infection, neoplasm and trauma, can cause this symptom complex.

REPORT OF CASES

The first patient, a man aged 72 years, was seen August 4, 1946. He complained of severe pain in the right eye and temperoparietal area, diplopia and impaired vision which began suddenly three days before his admission to the hospital. Examination showed ptosis of the right upper lid, slight proptosis, and the eyeball fixed in the straight ahead position. There was no redness, edema, tenderness or displacement of the orbital structures. The media were clear. The dramatic feature was the abrupt onset of impaired vision and complete paralysis of the ocular muscles of the right eye during the course of what was considered to be an ordinary bronchial cold. X-ray films revealed clouding of all of the sinuses on the right side and a very large (Fig. 2) sphenoid and frontal sinus. The bony structures of the right posterior orbital wall appeared indistinct, and the superior orbital fissure could not be clearly outlined.

TABLE I

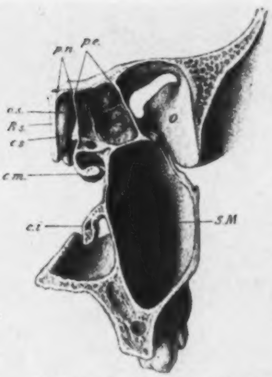
STRUCTURES THAT MAY BE AFFECTED BY DISEASE IN THE SPHENOID SINUSES

(Emphasized by Proetz[2])

IMPORTANT STRUCTURES EASILY DISTURBED BY SPHENOID DISEASE GIVING RISE TO VARIED AND PUZZLING SYMPTOMS

DURA	ABDUCENS N.
PITUITARY	OCULOMOTOR N.
OPTIC NERVE-CHIASM	TROCHLEAR N.
CAVERNOUS SINUS	OPTHALMIC N.
INTERNAL CAROTID A.	SPHENOPALATINE N.
PTERYGOID CANAL AND NERVE	MAXILLARY N.

ILLUSTRATION SEEN IN ORBITAL APEX OR SPHENOID FISSURE SYNDROME



Frontal section through the most posterior part of the posterior ethmoidal labyrinth (¾ natural size).

S.M., sinus maxillaris; *O.*, orbita; *c.i.*, concha inferior; *c.m.*, concha media; *c.s.*, concha superior; *R.s.*, rostrum sphenoidale; *o.s.*, ostium sphenoidale; *p.n.*, pars nasalis; *p.e.*, pars ethmoidalis of the anterior wall of the sphenoid sinus.

Fig. 1.—The anatomical basis for the etiology of the orbital apex syndrome in the antrum, ethmoid and sphenoid sinuses is illustrated by the contiguity of these sinuses with the apex of the orbit. (From Hajek[5])

The optic foramen showed no abnormalities. His response to penicillin was prompt. Within 48 hours the pain had disappeared, ptosis was less and there was movement of the eyeball. The eye returned to normal and the sinuses became clear with three weeks of penicillin therapy.

The second patient was a man, aged 46 years, whom I saw in January 1951. His symptoms were ptosis of the right eyelid, right occipital headache and double vision. The examination revealed about 6 mm of proptosis and limited movement in upward and lateral gaze with diplopia in all fields. Vision and tension were normal. Intranasal examination showed a small polyp on the right side but no purulent discharge. X-rays of the sinuses revealed a chronic sinusitis with some osteitis about the frontal sinuses. One week after admission a temperature of 102° occurred with congestion of the conjunctiva and edema of the upper lid. Under penicillin therapy all these symptoms receded and full ocular movement returned. He then developed fixation of the left eye (Fig. 3) due to ophthalmo-

Fig. 2.—Case 1. Roentgenogram showing cloudiness of the very large right sphenoid sinus, caused by acute infection.

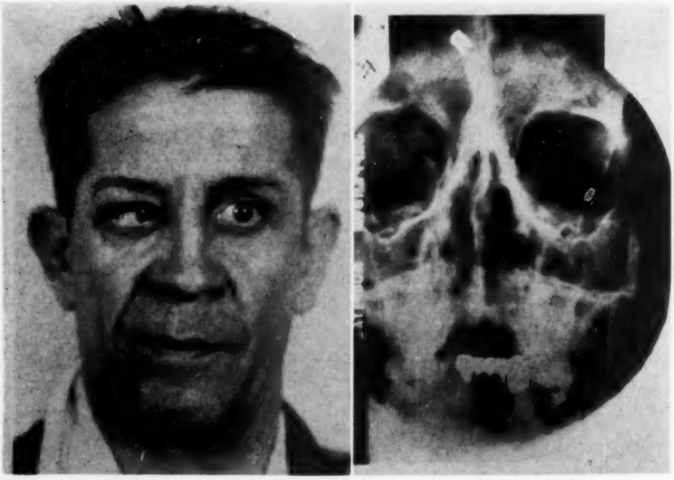


Fig. 3.—Case 2. Typical appearance of patient with orbital apex syndrome showing complete ophthalmoplegia of the left eye with the bulb fixed in the straight ahead position. Also x-ray of sinuses showing pansinusitis with osteitis about the frontal sinuses.

Fig. 4.—Case 3. Illustrating orbital apex syndrome of the left side due to carcinoma of the left ethmoid and sphenoid area. There is total blindness in the left eye and complete ophthalmoplegia. The only evidence of sinus disease was slight cloudiness of the left ethmoid sinus upon x-ray examination.

plegia, with a return of diplopia. Spinal puncture was negative. Penicillin therapy was resumed along with Proetz displacement and removal of the polyp. The patient improved but his diplopia remained due to persistent paralysis of the left VI nerve. In addition to the orbital apex syndrome some of the more common inflammatory orbital complications occurred in this patient.

The third patient was a 40 year old woman who was seen April 1952. Complete blindness and ophthalmoplegia of the left eye had occurred suddenly six weeks before on March 6. The only other complaint of significance was a moderate headache located in the left frontoparietal-occipital region which had been present about three months. The significant physical findings were all referable to the eye, namely; complete ophthalmoplegia and blindness due to impairment of the II, III, IV, and VI cranial nerve. There was some dilatation of the left pupil.

The x-ray examination revealed erosion of the medial margin of the lesser wing of the sphenoid and the anterior clinoid process, and

Fig. 5.—Case 3. Showing arteriographic study. The conventional knuckle of the internal carotid artery which is usually seen alongside of the pituitary fossa is absent and instead the more anterior segment of this curve is flattened out. It suggests a mass lesion at the junction of the floor of the anterior and middle cranial fossa.

slight evidence of ethmoidal sinusitis on the left side (Fig. 4). Arteriographic findings (Fig. 5) suggested the presence of a mass lesion at the junction of the floor of the anterior and middle cranial fossa. The x-ray finding of slight ethmoid sinusitis was not considered significant in view of the arteriographic picture which pointed to a retrobulbar lesion. At a conference of radiologist, ophthalmologist, neurologist and neurosurgeon it was concluded that a paraseller tumor was the most probable cause of the syndrome and intracranial surgery was decided upon. However, the clinical picture changed abruptly the following day when the patient suddenly and unaccountably developed epistaxis and the otolaryngologist was consulted.

His examination, after extreme shrinking of the mucosa with adrenalin, revealed a small granular mass in the left spheno-ethmoid area which was very vascular and bled readily when touched with a probe. The middle turbinate was removed and a tumor mass which involved the posterior ethmoid and sphenoid area was exposed. It proved to be a squamous cell carcinoma and was the cause of the symptom complex.

The fourth case involves more than the orbital apex syndrome in its clinical manifestations. However, it belongs in this discussion because it illustrates that lesions of the maxillary sinus as well as of the posterior ethmoid and sphenoid sinuses can involve the apex of the orbit and produce this syndrome.

The patient was a male, aged 59 years, who entered the hospital Receiving Ward in a toxic, lethargic state in August 1957. He complained of headache, stomach discomfort, nausea and right facial weakness. His response to questions was so vague that it was difficult to obtain a clear history. He was under treatment for diabetes in the out-patient department and had received treatment for lues some years ago. The main features of the examination were complete paralysis of the right VII nerve, severe pain in the right temporal region and behind the eye, lethargy, and a blood sugar of 240. Three days later blindness, complete ophthalmoplegia, a moderate degree of proptosis and numbness over the second division of the V nerve were present, in addition to the VII nerve paralysis (Fig. 6). There was no complaint referable to the nose or sinuses, and they were not considered to be a factor in the diagnostic problem until an incidental finding by the intern brought in the otolaryngologist to account for a small amount of freshly dried blood which was found in the right external auditory canal.

It had apparently resulted from puncture of the ear lobe for a blood count as examination of the ear was negative, and there was no impairment of hearing. However, examination of the nose for the first time revealed that the cause of the bizarre clinical picture was an extensive lesion of the nose and sinuses. The right naso-antral wall and turbinals appeared to be a mass of necrotic tissue which was covered by a yellowish, purulent crust and x-ray study showed marked clouding of the right maxillary, ethmoid and to a lesser

Fig. 6.—Case 4. Showing appearance of patient with blindness, complete ophthalmoplegia and complete peripheral VII nerve paralysis on the right side.

extent of the right frontal sinuses (Fig. 7). The sphenoids and mastoids were clear. The eyeball had become proptosed and injected, and the conjunctiva was edematous. External fronto-ethmoid and Denker operations were done, and the greatest amount of pathology was found in the maxillary sinus. Its anterior, orbital, and naso-antral walls were necrotic, and there was a large collection of pus in the canine fossa beneath the muscles. The anterior and posterior ethmoid sinuses were filled with pus and necrotic tissue. The right frontal sinus was partly filled with mucopurulent discharge, but the sphenoid sinus was clear. Involvement of the orbital structures had occurred primarily by extension of the lesion from the antrum

Fig. 7.—Case 4. X-ray showing marked cloudiness of the right maxillary, ethmoid and to a lesser extent the right frontal sinus.

through its roof, and posterior wall, and beyond to include the VII nerve. Microscopic study of the diseased tissue showed dense cancellous bone which was in part necrotic and heavily infiltrated by acute and chronic inflammatory cells. There were areas of acute collagenous necrosis and tuberculoid reaction with multinucleated giant cells of the foreign body type. The microscopic diagnosis was chronic granulomatous, paranasal sinusitis and chronic osteomyolitis.

The striking feature of this case is that a massive lesion of the sinuses and nose could develop and progress to such an extent, without any symptoms referable to them. The patient denied ever having had any trouble with his nose. The absence of sensation over the V

nerve was explained by the involvement of the maxillary nerve in the necrotic process. The necrotic nerve was suspended in the antrum like a rope. The basic lesion was apparently due to a slow necrosis of the tissues from avascularity caused by endarteritis and thrombophlebitis of diabetic or syphilitic origin, or possibly both. In reality, it was a gangrenous lesion similar to that which may occur in the extremities of older people as a complication of diabetes. The patient has recovered full ocular movement, but blindness and VII nerve paralysis still persist and are probably permanent.

The fifth patient illustrates the orbital apex syndrome caused by trauma.

He was a 22 year old enlisted man who fell from a high ladder hitting the frozen ground at Camp Dix on February 13, 1958. When he regained consciousness he was blind in the left eye and the eyeball was fixed in the straight ahead position due to complete ophthalmoplegia. In addition to other injuries, which are not pertinent to this discussion, he sustained fracture of the greater wing of the left sphenoid, lateral wall of the left antrum, floor of the left orbit, the anterior wall of the left frontal sinus and the medial portion of the left orbital roof near the cribriform plate. He recovered rapidly from the shock and immediate effect of the injury, and by March 13 full ocular movement had returned, but blindness persisted and signs of optic atrophy were present.

On March 13, one month after the accident, massive bleeding occurred suddenly and without warning from the left nasal chamber. It stopped within 15 minutes before the nose could be adequately packed. During the next 16 days he had five more episodes of sudden profuse nasal hemorrhage from the left side. Ligation of the left external carotid artery and a Caldwell-Luc exposure of the left antrum were done in a futile effort to find the origin of the bleeding. During this time the patient was transferred to the Valley Forge Army Hospital where he was seen in consultation on April 3. He was then ambulatory, and in good general condition. Firm bilateral anterior and postnasal packs were still in place following the last severe hemorrhage on March 9. Complete blindness of the left eye was still present but there was no impairment of ocular movement. It was my opinion that the bleeding had occurred from the internal carotid artery and had reached the nasal chamber through a fracture of the thin wall sep-

arating it from a large sphenoid sinus indicated by x-ray film. The neuro-surgeon, however, insisted that its origin was extracranial; probably from ethmoid vessels. The nasal packs were removed and there was no further bleeding. Two days later, April 13, paralysis of the right lateral rectus appeared, and there was a bradycardia of 50-60. The eye symptoms progressed and by April 15 the complete orbital apex syndrome was present on the right side with ptosis of the right upper lid, complete ophthalmoplegia, and impaired vision.

On this day he was transferred to Walter Reed Army Hospital with a probable diagnosis of arteriovenous aneurysm involving the internal carotid artery and the cavernous sinus.

SUMMARY

The orbital apex syndrome is a symptom complex that may be produced by a lesion behind the orbit, or it may occur as a complication of sinus disease. Examples of this syndrome caused by infection, neoplasm, and trauma of the ethmoid, sphenoid and maxillary sinuses have been presented by a brief review of the clinical records of five patients. These patients illustrate that this syndrome when due to a sinus lesion, may appear suddenly as the only clinical manifestation of the disease, and when it occurs a careful search of the sinuses for its etiology is urgent because it is usually a warning of serious trouble.

1830 Spruce St.

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Scientific Papers of the American Otological Society

LVII

THE HYDRODYNAMIC ORIGIN OF AURAL HARMONICS IN THE COCHLEA

JUERGEN TONNDORF, M.D. (by invitation)

IOWA CITY, IOWA

This paper presents a hypothesis concerning the intracochlear origin of harmonic distortion. This hypothesis is based upon experiments in cochlear models and in guinea pigs. Before taking up this subject in detail, a few words may be in order about harmonic distortion in general.

Ideally, a system when undergoing forced vibrations reproduces exactly the impressed waveform. For instance, for an impressed sinusoidal waveform a system executes sinusoidal vibrations of the same frequency. The amplitude must not necessarily be equal to that of the driving system. However, if the amplitude of the latter is altered, the amplitude of the driven system will change proportionally. This ideal condition is only met at relatively small ampitudes as long as Hooke's law* applies. This law states that the *stress is proportional to the strain* within the limits of elasticity. However, at higher amplitudes this relation ceases to be linear. Therefore, the resultant waveform becomes disfigured, i.e., distorted. According to Fourier's theorem, any waveform can be analyzed into a series of simple (sinusoidal) vibrations. In the case of nonlinearity, these newly formed partials are in harmonic relation to the original frequency, the fundamental. Therefore, the terms nonlinear and harmonic dis-

* Originally, Hooke (1664) gave the law named for him by the following anagram in Latin: "Ut tensio, sic vis" (as the tension so is the force). (From R. T. Gould: The Marine Chronometer; Its History and Development, London, 1923)

tortion are often used synonymously. Figure 1 shows some examples of such distortion. The waveforms in the two upper cases (A and B) of this figure are distorted in a symmetrical manner with reference to the base line, whereas in case C distortion as asymmetrical. (The reason for this difference is simply that in one case the limits of elasticity are reached symmetrically in both directions of displacement and in the other they are not.) A Fourier analysis indicates that symmetrically distorted waveforms contain a series of add harmonics, whereas asymmetrical waveforms contain even harmonics.

Harmonic distortion is inherent to all vibrating systems, mechanical as well as electrical, since all of them possess an elastic or equivalent limit. Different systems may vary only in the width of the range before distortion occurs, that is, in the width of their dynamic ranges. The peripheral ear is essentially a mechanical, vibrating system, up to the level of the haircells. Therefore, it produces harmonic distortion when stimulated beyond certain amplitudes. The question whether or not such distortion might arise in the neural portion of the auditory system can be negated; for here the signal never consists of trains of waves but of series of pulses. Overdriving a system generating and transmitting pulses produces entirely different results which need not be discussed here.

It is the consensus of opinion, therefore, that aural harmonics must be a property of the peripheral ear. Helmholtz,[8] who first explained their origin on the basis of nonlinearity, believed the middle ear to be the exclusive locus of origin. However, later clinical and experimental data[2,9,16] showed that, granted this might be true, distoration was also occurring in the inner ear and that this intracochlear distortion occurred at an intensity level lower than that in the middle ear. Such observations were hard to reconcile with Helmholtz's concept of the cochlea acting like a series of tuned resonators. However, the advent of the traveling-wave concept of cochlear stimulation, mainly through the experimental work of von Bekesy,[1] has made intracochlear distortion a plausible entity. There is strong indication that this distortion originates in the hydrodynamical events accompanying the displacement of the basilar membrane.

For purposes of experimentation on cochlear hydrodynamics, cochlear models after Bekesy are best suited. Such models can be made of transparent plastic (Fig. 2) containing two perilymphatic

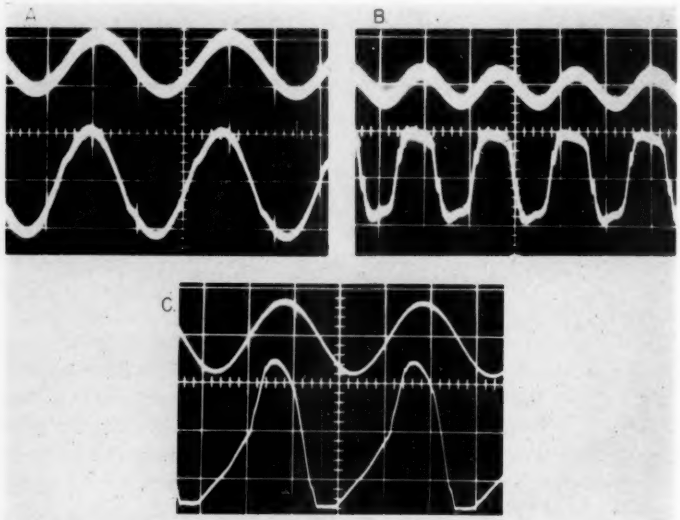

Fig. 1.—Three examples of nonlinear (harmonic) distortion. In each case the waveform is given before (top) and after (bottom) distortion. A and B: Symmetrical distortion (note presence of 3rd harmonic): A: moderate; B: more severe distortion; C: asymmetrical distortion. All these waveforms were produced by deliberate overloading of electronic amplifiers.

scalae and a partition with a (basilar) membrane elasticity of which decreases toward the helicotrema. These membranes are made of rubber cement. Suspension of small particles of aluminum in glycerin-water solutions facilitate observation and photography of fluid motion. The model is driven by a loudspeaker driver unit which is coupled to the oval window by a small closed and air-filled coupler. A stapes need not be there as its presence is unessential to the problem under investigation.

The most conspicuous among Bekesy's findings with respect to the generation of harmonic distortion was the fact that the displacement of the basilar membrane is accompanied by a symmetrical pair of eddies on both sides of the cochlear partition. Bekesy himself has voiced the opinion that these eddies might be responsible for

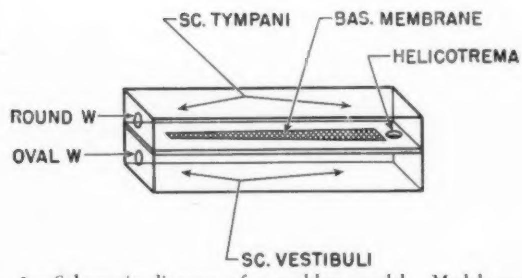

Fig. 2.—Schematic diagram of a cochlear model. Models used in the present study were 2x to 5x larger than natural size.

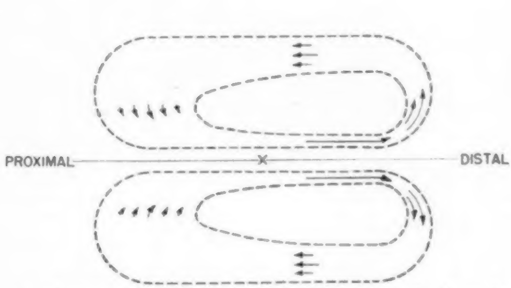

Fig. 3.—Pattern of eddy motion in both perilymphatic scalae (schematic). The (x) indicates the locus of maximal displacement of the basilar membrane. Note: In reality, the eddies do not have a static center as might appear from this graph.

the production of harmonic distortion in the cochlea. The present author was able to support this opinion by the following two observations in cochlear models:[13] 1) the displacement of the basilar membrane starts at an intensity level lower than that at which the eddies first appear. Also, the membrane displacement is proportional to the amplitude of the driving force, whereas the average revolving velocity of the eddies is a function of the square of this amplitude; 2) particle motion within the cochlear fluids in the region where it is superimposed upon the eddies showed a cumulative phase lag much in the same manner as that occurring in the displacement wave along the cochlear partition originally observed by Bekesy. The total of this phase lag, once around the eddy, was exactly 360° or one

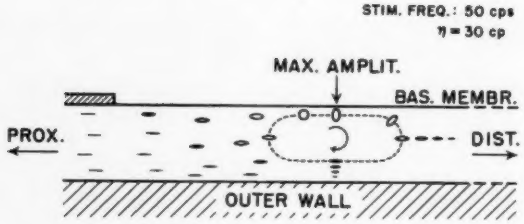

Fig. 4.—Pathways of particle motion and their variation at different locations within the fluids of one perilymphatic scala (from reference 13).

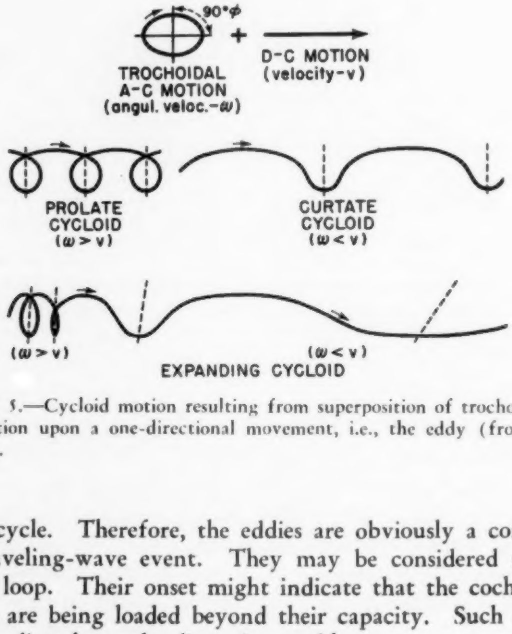

Fig. 5.—Cycloid motion resulting from superposition of trochoidal particle motion upon a one-directional movement, i.e., the eddy (from reference 14).

complete cycle. Therefore, the eddies are obviously a continuation of the traveling-wave event. They may be considered a bilateral feed-back loop. Their onset might indicate that the cochlear fluids and scalae are being loaded beyond their capacity. Such considerations point directly to the distortion problem.

Next, the eddies and the superimposed particle motion must be reviewed in some detail. The eddies revolve in a manner indicated in Figure 3. As schematically shown in this graph, their revolving

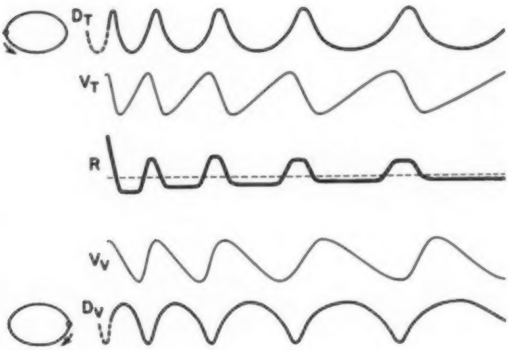

Fig. 6.—Bilateral effect of expanding cycloid motion upon the displacement of the basilar membrane (schematic). DT & DV: displacement pattern in scala tympani and scala vestibuli in proper phase relationship (cf. orbits at left side); VT & VV: velocity patterns of DT & DV; R: resultant of VT & VV, i.e., the effect upon the displacement of the basilar membrane (from reference 14).

velocity is not uniform. There is a sharp acceleration along the partition which reaches its highest value at the point where the eddy turns away from the membrane. Thereafter, a deceleration takes place which continues throughout the return path. This pattern of acceleration is accompanied by an according narrowing and widening of the eddy's bed as is also shown in Figure 3.

The primary event upon vibratory stimulation of the model is not the eddy (which was said to come into existence only at higher amplitudes of the driving force) but an alternating (to and fro) motion of the cochlear fluids originating from the oval window. However, the fluid does not simply move en bloc like a piston of liquid but its particles undergo quite different modes of motion in the various regions of the perilymphatic scalae. Therefore, this motion is best referred to as the particle motion within the cochlear fluids. Its pattern is given in Figure 4. Motion is seen to be purely longitudinal in the vicinity of the window; but as soon as the region of the (yielding) basilar membrane is reached elliptical orbits appear. Along these orbits particles whirl around, once during each vibratory cycle. The direction of rotation happens to be the same as that

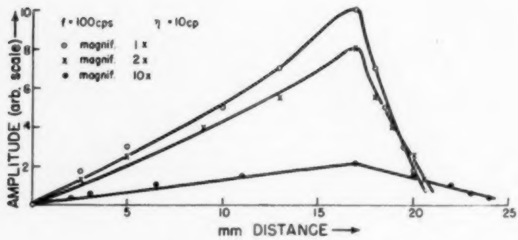

Fig. 7.—Envelopes over the traveling-wave event along the cochlear partition at three different amplitude levels. Measurements were facilitatd by the use of different degrees of magnification as indicated (from reference 14).

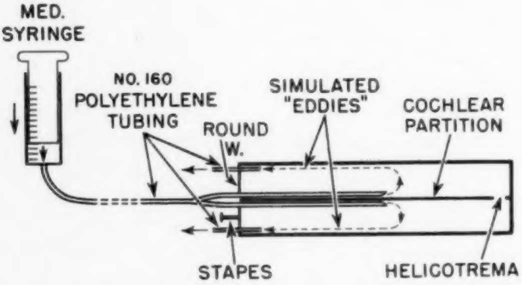

Fig. 8.—Arrangement for production of artificial addies of varying velocity, while the driving intensity is kept constant (schematic from reference 14).

of the eddy (cf. arrow in Figure 4) upon which particle motion is superimposed undergoing further changes which need not be discussed here. (The interested reader is referred to reference 13.) The pattern of motion in the other perilymphatic scala which is not shown in Figure 4 is an exact mirror image of that presented in the graph, that is, it is lagging 180° in phase at all corresponding points.

The nature of the elliptical orbits is revealed in the top left-hand drawing of Figure 5. Such orbits are brought about by the presence of two forces acting in different directions. It is customary to express

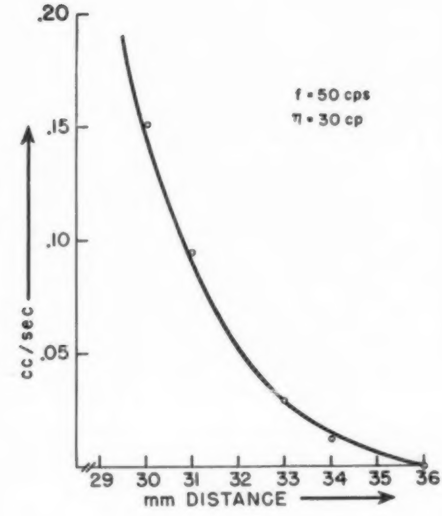

Fig. 9.—Velocity of the artificial eddies necessary to produce alterations in length of the envelope over the traveling waves along the cochlear partition (from reference 14).

the magnitude and direction of such forces by so-called vectors, i.e., arrows of given length and direction. In the case at hand, these vectors express the (original) window motion and the (induced) displacement of the basilar membrane. (In Figure 5 the arrowheads are omitted since the motion is alternating.) These two vectors are perpendicular to each other, as can be inferred from Figure 4, or, since the motion is of a vibratory nature, may be said to be 90° apart in phase. Such orbits which result from the interaction of two vectors and need not necessarily always be elliptical, as will be seen later, are known as Lissajou figures.

Obviously, the presentation of Figure 4 does not indicate the true pathways of particles as they are propelled around the eddy's course. The superposition of a trochoidal motion upon a one-directional movement results in a cycloid form of motion as is shown in Figure 5.

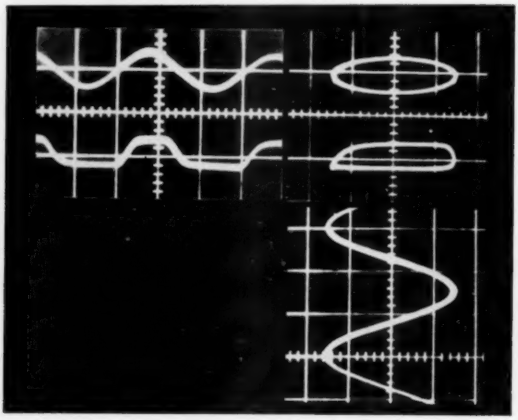

Fig. 10.—Construction of Lissajou figures from two vectors slightly less than 90° apart (from actual oscillographic recordings). Upper figure: both vectors sinusoidal; lower figure: one vector peak clipped and asymmetrical (from reference 14).

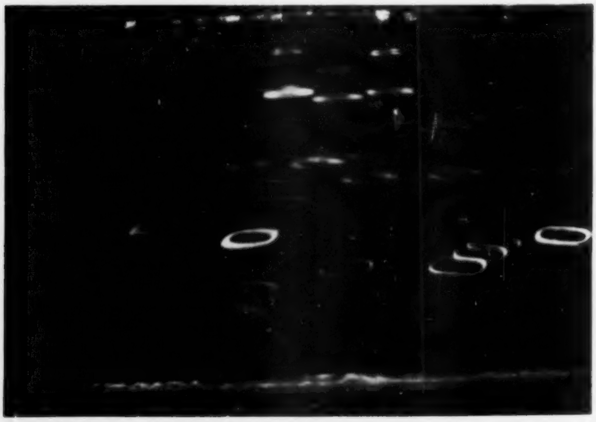

Fig. 11.—Particle orbits photographed in the tympanic scala in response to an impressed sinusoidal waveform in the presence of strong eddy motion. The basilar membrane is on the bottom, proximal is on the right, distal on the left; the eddy moves clockwise. Note sign of asymmetry at the distal end of the eddy.

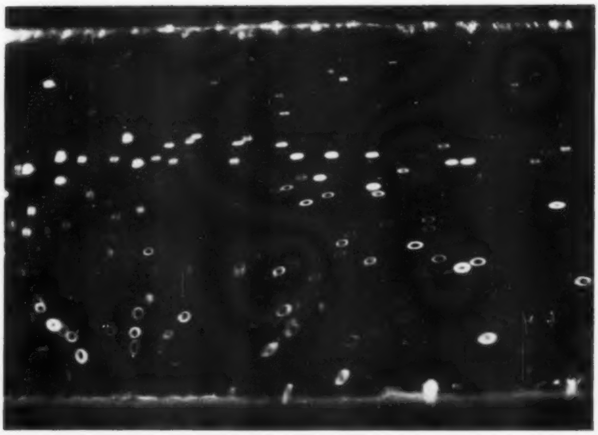

Fig. 11a.—Same as in Figure 11, except at lower driving amplitude below the onset of eddy motion. Compare with Figure 11 and note difference of particle orbits in the two cases.

Depending upon the rate of the velocities of both motions, either prolate or curtate cycloids will result. However, if the one-directional movement is accelerating, as it does in the case of the eddies, expanding cycloids are produced.

This expanding form of cycloid motion takes place on both sides of the cochlear partition. Its effect upon the displacement pattern of the partition is schematically shown in Figure 6. This presentation is simplified in that only the curtate form of cycloids is shown and in that the alteration of the traveling-wave event with distance along the partition (Fig. 7) is neglected. The top and bottom rows of Figure 6 show the pattern of particle displacement in both perilymphatic scalae in their proper phase relation, which is 180° apart. Since it is known that the membrane responds to the velocity of the fluid displacement,[13] the next two rows (V_T and V_V) show the velocity pattern which is 90° ahead in phase with respect to the displacement, representing itself as an expanding sawtooth waveform. Finally, the combination of both velocity patterns, the resultant R, indicates the effect upon the displacement of the basilar membrane.

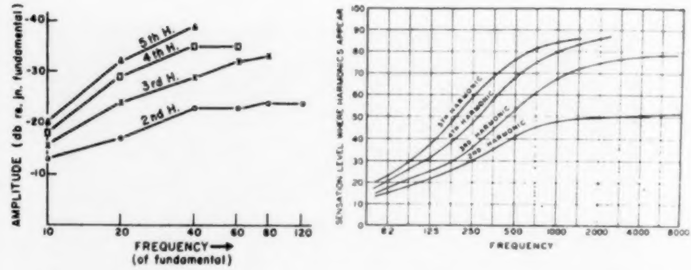

Fig. 12.—Left amplitude (re. onset of fundamental) at which harmonics (2nd to 5th) are first noted for several low-frequency fundamentals (from reference 14). Right—audible onset of harmonic partials in terms of sensation level vs. frequency of fundamental (adapted from Fletcher[7]).

Three phenomena are apparent from Figure 6: 1) a decrement of amplitude with distance; 2) peak clipping; and 3) an asymmetry, the displacement toward the tympanic scala being larger than toward the vestibular scala.

These theoretical results had to be corroborated by experimental facts. A decrement of amplitude with distance should reflect upon the shape of the envelope over the traveling-wave event along the cochlear partition. According to Bekesy,[3] this envelope is asymmetrical, its distal slope being steeper than the proximal one. Three such envelopes were measured at different amplitude levels which was facilitated by means of using different degrees of microscopic magnification. The results of these measurements are presented in Figure 7. It is apparent that the distal slope becomes steeper and shorter with increasing amplitude suggesting that at very small amplitudes the envelope might be more nearly symmetrical. Needless to say, the velocity of the eddies increased with each increase in amplitude, while these measurements were being taken. In order to determine the possible influence of the eddies upon this alteration of the envelope, a method was devised by which artificial eddies of varying velocity were introduced into the model, while the driving amplitude was kept constant. The arrangement used is shown in Figure 8. It then was found that the envelopes became shorter when the velocity of the artificial eddies was increased (Fig. 9). This result demonstrated that it was indeed the eddies which were responsible for the alteration

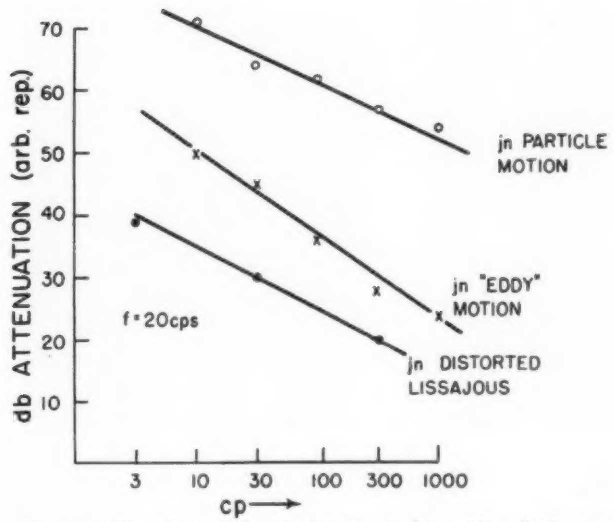

Fig. 13.—The effect of altered viscosity of the cochlear fluids upon the onset of a) particle motion b) eddy motion; c) distorted Lissajous (from reference 14).

of the envelope shown in Figure 7. In turn, the alteration of the envelope represents the postulated decrement of amplitude with distance.

The existence of peak clipping and of asymmetry, the two other postulates, was proven by a different method. It was recalled that particle orbits as shown in Figure 5 (top) are actually Lissajou figures. Alteration of the waveform of one vector should therefore reflect upon the shape of such Lissajou figures. Shown in Figure 10 are two Lissajou figures, the top one caused by interaction of two vectors of sinusoidal waveform resulting in the (normal) elliptical shape. (The vectorial phase relation is slightly less than 90° which is typically observed within the distal portions of the eddies.) In the lower case of Figure 10, one of the vectors was peak clipped and made slightly asymmetrical. The resulting Lissajou figure is characteristically flattened. If the vectorial phase relation were exactly 90°, the left and right sides of this Lissajou would be symmetrical, being slightly wider

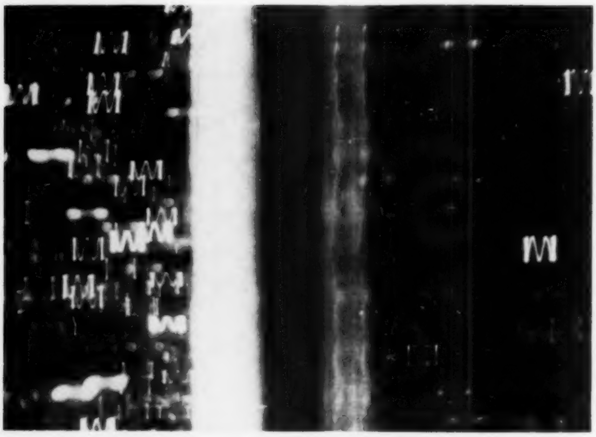

Fig. 14.—Waveform of longitudinal particle motion in both perilymphatic scalae (tympanic sc. lighter!) close to the windows. Waveform was obtained by sliding the photographic film within the camera in a direction transversal to the cochlear partition. Note identical waveform but phase difference of 180° between the two scalae. While this sinusoidal waveform was obtained, particle orbits along the eddies were flattened. Frequency: 15 cps. Photographs had to be taken at low frequencies, since at higher frequencies particles moved too fast and did not produce tracings bright enough for photographic purposes.

on the bottom than on the top. As it is, the Lissajou is drawn out slightly at one of its four corners.

Figure 11 shows an actual photograph of particle orbits in response to an impressed sinusoidal waveform, but in the presence of strong eddy motion. Such flattened particle orbits had always been seen before but had been thought to be introduced by extraneous distortion, before their mechanism was understood. If properly analyzed, these particle orbits show both peak clipping and asymmetry, indicating the presence of odd and of even harmonics.

This distorted hydrodynamical pattern is resolved along the cochlear partition in accordance with the place principle of frequency localization. Each harmonic forms its maximum at its appropriate

place (that is, at the same place where it is formed when the same frequency is applied to the model as an independent pure tone.) Figure 12 (left side) gives the amplitudes at which the onset of various harmonics (each at its appropriate place) is first noted for several low frequencies. The accompanying graph (Fig. 12, right side) is taken from Fletcher[7] and shows the audible onset of harmonic partials in terms of sensation levels. The similarity between the results obtained from the model and the psychophysical data is striking.

The reason for the peculiar relationship between frequency and the onset of harmonics in both graphs of Figure 12 lies very likely in the fact that the average velocity and the size of the eddies vary both inversely with the square of frequency.[14] It is apparent from the theoretical considerations made in connection with Figures 5 and 6 that the appearance of flattened particle orbits is governed by the average velocity and by the size of the eddies, i.e., by the acceleration along the basilar membrane and by the distance over which the acceleration is effective.

Proof was obtained in several ways that the distortion described here had not been introduced extraneously but had actually originated within the model. It will suffice here to cite one example. Figure 13 shows that alteration of the viscosity of the cochlear fluids affects the onset of distorted Lissajous in a similar manner as that of particle and of eddy motion (although at different levels.) If the distortion had been extraneous, no such dependence would exist.

Wever and Lawrence[17] have advanced a theory, concerning the origin of intracochlear distortion, which substantially differs from the hydrodynamical theory presented here. They had concluded that this distortion should occur beyond the cochlear fluids at the level of the haircells because of the following observation they had made:[16] distortion, which had been present in the cochlear microphonic response of a cat's ear, did not make its appearance in the mechanical movement of the round-window membrane of the same ear under identical conditions. However, this finding of theirs is precisely what one must expect from the standpoint of the hydrodynamic hypothesis: the appearance of distortion must be limited to the pathways of the eddies. In the model, intracochlear distortion did not affect the

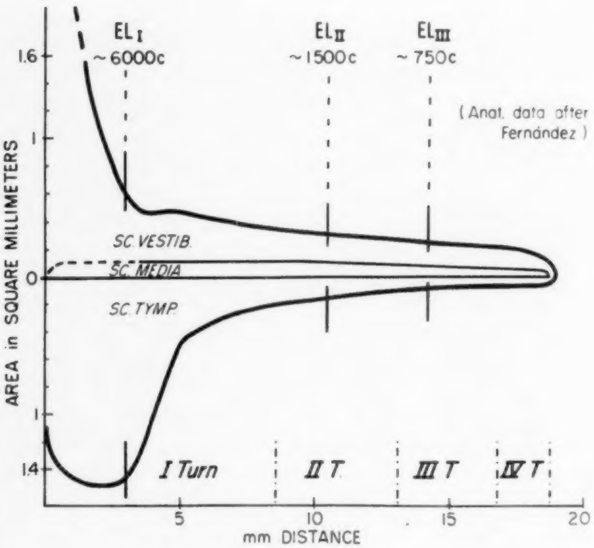

Fig. 15.—Schematic outline of an unrolled guinea pig's cochlea (anatomical data after Fernandez[6]). Differential electrodes inserted in basal, 2nd, and 3rd turns. Frequency of maximal responses at these points approximately as indicated (from reference 15).

motion of the round-window membrane either. Evidence is given in Figure 14 which shows that identical waveforms exist on both sides of the cochlear partition in the immediate vicinity of the windows. When these waveforms were photographed, distortion was clearly present along the pathways of the eddies.

The respective validity of the haircell and of the hydrodynamic hypotheses can be tested from a different aspect by means of recording cochlear microphonic responses in laboratory animals.

For a number of years, a method has been used whereby cochlear microphonics have been recorded by means of differentiating electrodes.[4,12] By this is meant that instead of the customary single active electrode placed at the round window, two such electrodes are inserted at corresponding points on both sides of the cochlear duct, i.e., one

in the vestibular scala and the other in the tympanic scala. A third (ground) electrode is connected to the neck muscles. It has been mentioned before that there is a phase relationship of 180° between two such points with regard to the mechanical movement of the partition and the cochlear fluids. The same applies to cochlear microphonic responses. Among the advantages derived from the use of such electrodes are a) rejection of unwanted (out-of-phase) signals, e.g., 60c hum, and b) limitation of the area from where cochlear microphonics are picked up to approximately 1 mm length of the basilar membrane.[11] Tasaki, Davis, and Legouix[10] inserted up to six pairs of differentiating electrodes at various points along the cochlea thus mapping the cochlear microphonic responses as to amplitude and phase. Their results indicated that the generation of microphonics along the cochlea is in close agreement with Bekesy's observations of (mechanical) traveling-wave phenomena.

This method of recording cochlear microphonics was adopted for the purpose of further differentiation between the two hypotheses concerning the origin of intracochlear distortion. The following reasoning was made: if the harmonics were generated by the haircells (according to Wever and Lawrence), higher harmonics should be recorded at a constant amplitude ratio to that of a fundamental of given frequency and amplitude, wherever this fundamental was present along the cochlea. However, this would not be the case, if the harmonics were generated hydrodynamically and if resolution along the basilar membrane were in accordance with the place principle. Each harmonic would then set up a traveling-wave pattern of its own so that for simultaneous recordings from several points the waveform should differ as to amplitude, harmonic content, and phase relation among partials.

Differentiating electrodes were inserted in the basal, 2nd, and 3rd turns of a guinea pig's cochlea (Fig. 15). Of the results obtained, only two will be discussed here. 1) Gradient curves were assessed (i.e., curves depicting input intensity vs. output voltage). At various pick-up points, their shape was not identical, a fact already noted by Tasaki et al.[10] These gradient curves as shown in Figure 16 were linear over a wider range (with respect to input intensity) in the basal turn, i.e., at the entrance to the cochlea, but became increasingly nonlinear as the locus of that particular frequency was approached. (The improved linearity after that point may be partially accounted

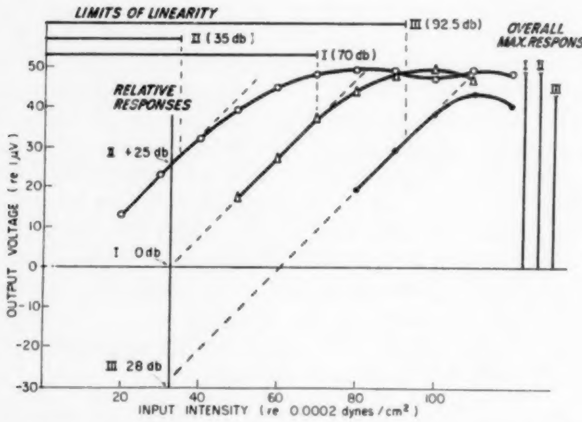

Fig. 16.—Gradient curves of cochlear microphonics recorded in 1st, 2nd, and 3rd turns. Note difference in relative and over-all (maximal) responses, and in linearity (the latter with respect to input intensity). In this particular test, the locus of the frequency used (200 cps) was just proximal to the electrode in turn 2.

for by the loss in over-all response.) This observation means that the *distortion at the point of maximal response is of intracochlear origin.* Distortion at the cochlear entrance (presumably generated in the middle ear) appears at higher intensity levels. 2) Response curves (for constant input intensity) were assessed which showed a distinct maximum indicating the locus of the frequency which was closest to the pick-up point. Such response curves were obtained for the fundamental, the second, and the third harmonic for a series of frequencies and by means of narrow-band filtering. A typical example of such recordings for one pair of electrodes is given in Figure 17. It is apparent from this figure that *the maximum is always formed at the same frequency location regardless of whether the frequency is present as a fundamental or as a newly generated higher harmonic.* These and other results not mentioned here but published elsewhere[15] are in good agreement with the hydrodynamic hypothesis and do not confirm the haircell theory of the origin of intracochlear distortion.

After the description of the experimental results, a brief comment might be in order concerning the physiological significance of

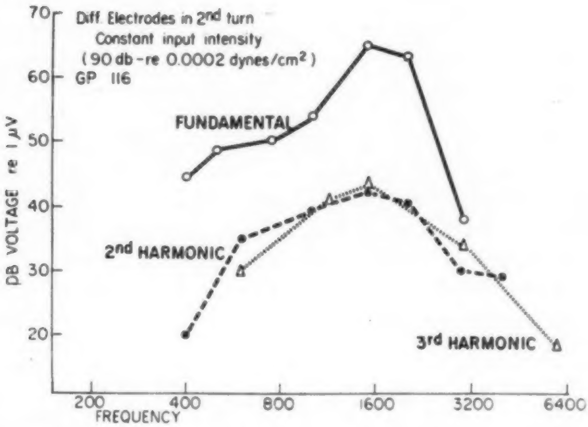

Fig. 17.—Response curves recorded from differential electrodes in turn 2 for fundamental, 2nd, and 3rd harmonic, obtained by means of narrow-band filtering.

intracochlear distortion of hydrodynamic origin. Discussing a recent paper by Lawrence on the "Aural Overload Test," Davis[5] made the remark that intracochlear distortion might be a protective measure rather than a potentially injurious event, as the term "overload" might imply. Davis had simply reasoned that a phenomenon which has its onset 40-50 db above threshold, as it does, cannot represent overloading in its accepted sense, since this onset is about at the level of conversational speech, that is, in the middle of the physiological range of hearing. This interpretation can be supported by facts derived from the present study.

The essential phenomena in the hydrodynamic generation of intracochlear (harmonic) distortion are Bekesy's eddies. Earlier in the present paper the conclusion had been reached that the eddies are bilateral feedback loops for feeding back energy not expended on its travel toward the cochlear apex. This must certainly be considered a protective phenomenon. Establishment of the eddies might prevent the occurrence of standing waves which otherwise would occur for certain frequencies. One reason that eddies instead of

standing waves are formed might be in the different orientation of particle motion in the inbound and rebound portions of the eddies. It was indicated in Figure 4 that particle motion along the partition is predominantly oriented in a transversal direction, whereas in the return path particles regain their (original) longitudinal orientation. Thus two trains of waves exist which cannot form standing waves with each other because of their different forms of wave motion. Finally, transition of energy within the eddies occurs smoothly as indicated by the fact that the cumulative phase lag of particle motion throughout the eddies is precisely 360°. There is no indication of turbulence anywhere which would represent a potentially dangerous phenomenon. Additional information as to the details of the experimental procedure and further supporting evidence are contained in references 13, 14, and 15.

SUMMARY

According to experiments in cochlear models, intracochlear distortion is caused by Bekesy's eddies which transform the trochoidal particle motion within the perilymphatic fluids into a cycloid form of movement. The bilateral effect of this cycloid motion upon the basilar membrane produces: 1) an amplitude decrement with distance; 2) peak clipping; 3) an asymmetry, displacement toward the tympanic scala being wider than toward the vestibular scala.

The amplitude decrement causes the envelope over the traveling waves along the cochlear partition to alter. The distal slope of the envelope becomes shorter and steeper with increasing eddy velocity. The peak clipping and the asymmetry reflect upon the pattern of particle motion within the perilymphatic fluids. This distorted hydrodynamical pattern is resolved along the cochlear partition in accordance with the place principle of frequency localization, but is confined to the pathways of the eddies.

These model observations were supported by findings in guinea pigs concerning cochlear microphonic responses. Evidence was obtained that distortion is actually produced within the cochlea at a lower level than in the middle ear: distortion was found maximal at the locus of each frequency along the basilar membrane. Further, the newly generated higher harmonics formed traveling waves along

the cochlea in the same manner as did the fundamental frequencies, forming maximal responses in accordance with the place principle of frequency localization.

UNIVERSITY HOSPITALS

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LVIII

DESTRUCTIVE LABYRINTHOTOMY: STUDY OF PROGNOSIS OF POSTOPERATIVE DISABILITY

KINSEY M. SIMONTON, M.D.

AND

PASCHAL A. SCIARRA, M.D. (by invitation)

ROCHESTER, MINN.

Considerable literature has accumulated regarding the technique and results of various surgical procedures devised for treatment of Ménière's disease refractory to medical therapy. All procedures have one aim in common, namely, interruption of the flow of nervous impulses from the disturbed vestibular labyrinth which cause episodes of vertigo, and all procedures have been successful in this regard.

The labyrinths are paired organs, each opposed to the other. When physiologically stimulated by movement of the head, a dominant response from one labyrinth is balanced by a minimal response from the other. The sum of the two responses combined with ocular and proprioceptive impulses provides the individual with knowledge of his position in space which is manifested as equilibrium. Interference with any one of the three sources of information impairs equilibrium, although the severe equilibrial storms which are referred to as vertigo result only from dysfunction of the labyrinth.

Surgical interruption of abnormal impulses from a diseased labyrinth has been proved to be a practical means of eliminating episodes of severe vertigo. The elimination of all impulses from one labyrinth alters the sum total of information providing knowledge of position in space and can be expected to produce disturbances of equilibrium. This disturbance is manifested by sustained vertigo in the period immediately following surgical interruption of labyrinthine impulses.

The human organism possesses remarkable powers of accommodation to changed conditions. Accommodation following surgical destruction of one labyrinth is manifested by progressive decrease in the severity of symptoms of impaired equilibrium. Following operation sustained vertigo becomes progressively less severe. The period of sustained vertigo is followed by a period in which the patient experiences vertigo only on motion. As accommodation progresses many patients become completely free of disturbance of equilibrium; others, however, fail to achieve complete recovery.

The literature which we have reviewed[1-6] suggests that the function of the operated labyrinth is the dominant factor in estimating duration of disability and degree of recovery to be anticipated following unilateral surgical destruction of the labyrinth.

Day[2] stated, "The duration of postoperative vertigo and imbalance varied in direct proportion to the amount of labyrinthine activity in the affected ear before operation as shown by caloric tests." In concurrence with this concept, Cawthorne[1] made the following statement: "The degree of postoperative disturbance has been largely governed by the amount of function present in the affected labyrinth before operation. With little function before, there is likely to be but little disturbance afterwards." This concept is logical if one accepts the hypothesis that the uninvolved labyrinth compensates for the functional loss of its partner. The dynamics by which compensation occurs remains a mystery.

One would, therefore, expect the period of rehabilitation to be shortest in those cases in which caloric stimulation of the involved ear elicits no reaction. Such a patient would be said to have a "dead labyrinth." In this situation, especially if it existed for a reasonable length of time before operation, one would expect the process of compensation to be in operation and with surgical destruction of the involved labyrinth the completion of compensation would ensue in a short time.

Even though a labyrinth fails to respond to caloric stimulation, some function still remains. It is this vestige of function that is responsible for the attacks of vertigo suffered by the patient which are eliminated by surgical destruction of the affected labyrinth.

This study was undertaken principally in an endeavor to corroborate the conclusions of the above-mentioned workers and also to determine, if possible, some other means by which the physician might predict the duration of postoperative adjustment.

Case material taken from the files of the Mayo Clinic was supplemented by a questionnaire. Destructive labyrinthotomy was performed on 97 patients over the nine-year period 1945 through 1953. Of this number, 20 were lost to follow-up. The material to be presented deals with the remaining 77 patients.

The factors selected for study are:

1. The age at the time of operation.

2. The duration of symptoms of vertigo.

3. The labyrinthine function. This was determined primarily by cold caloric testing. In the main the test employed was the modification of the minimal caloric test of Kobrak, as described by Williams. When no response was elicited by this technique the turning tests of Bárány were used to support the findings.

4. The cochlear function. This was determined by pure-tone audiometry supplemented by tests for recruitment, diplacusis, speech reception and pain threshold. Deafness is considered as of either nerve type or end-organ type. It is considered end-organ deafness if hearing tests demonstrated one or more of the following characteristics: a) base deafness or a flat threshold curve on pure-tone air-conduction audiometry, b) complete or hyperrecruitment, c) decrease in discrimination for the phonetically balanced words when presented at intensities greater than the most comfortable loudness, d) threshold of pain at intensities of 100 decibels or lower and e) diplacusis binauralis disharmonica as determined by tuning forks or audiometer.

5. The method of labyrinthine destruction. In all of our cases the goal of the surgical procedure was directed toward abolition of labyrinthine function. A variety of methods and combinations of methods were employed to accomplish this end. Essentially, they are avulsion of the membranous lateral semicircular canal, curettement of the ampulla of the lateral canal and the vestibule, electrocoagula-

tion of the vestibule, and the placing of bone chips into the ampulla of the lateral canal and the vestibule after one of the above methods has been carried out. In one case, Lempert's technique of destruction of vestibular contents through the oval window was performed.

The five postoperative factors studied are:

1. The number of days spent in the hospital.

2. The number of work days lost. This represents the number of days from operation until return to full activity.

3. Postoperative vertigo. The responses are classified into four groups (referred to as classes I, II, III and IV respectively in Tables VII to X): a) Complete stability. These patients are not only free from vertiginous attacks, but free from imbalance on quick motion, giddiness, or lightheadedness, and fear of impending vertigo. We feel that these patients have made complete adjustment, and now possess normal equilibrium. b) Instability without dizziness. These patients are free from vertiginous attacks and dizziness on quick motion, but experience a sense of imbalance, giddiness, or lightheadedness or combinations of these as a result of variety of conditions. The most frequent source of this symptom is darkness. Equilibratory symptoms are also ascribed to fatigue, undue exercise, head colds, minor illnesses, and standing on heights. Some patients complain of staggering when walking with the head turned to one side. c) Dizziness. These patients are free of vertiginous attacks but experience dizziness on quick motion. As a rule, they have made satisfactory adjustment and have learned to move in such a manner as to minimize the symptom. d) Recurrent attacks. These patients continue to have attacks of vertigo.

4. Postoperative tinnitus. Patients were asked whether tinnitus was absent or present, whether, if present, it was less, the same, or greater in loudness, and whether its character had changed.

5. Postoperative hearing.

The postoperative data in this series are summarized in Table I. Hospital stay varied from 4 to 14 days, the mean being 8 days. Of 65 patients reporting on duration of disability, 22 returned to full activ-

TABLE I

SUMMARY OF RESULTS OF LABYRINTHOTOMY

HOSPITAL DAYS	Mean, 8; range 4-14					
	WORK DAYS LOST					
	1 - 30	31 - 60	61 days - 4 mo.	5 - 12 mo.	No report	
Patients	22	22	11	10	12	
	VERTIGO, CLASS					
	I	II	III	IV		
Patients	22	27	24	4		
	TINNITUS					
	ABSENT*	ABOLISHED	REDUCED	SAME	INCREASED	NO REPORT
Patients	4	11	28	20	11	3

* Before and after operation

ity within 30 days of operation, 22 lost from 31 to 60 days, and the remaining 21 were disabled for periods of 61 days or more. More than half of the last group returned to full activity within 4 months after operation.

Twenty-two patients (29 per cent) are completely free of vertigo and have normal equilibrium. Twenty-seven patients (35 per cent) are free of vertigo and dizziness but experience disequilibrium at times. Twenty-four patients (31 per cent) have no vertigo but feel dizzy on quick motion. Four patients (5 per cent) continue to have episodes of vertigo. Of these, two developed symptoms referable to the unoperated ear one and four years respectively after operation, one was known to have bilateral involvement as well as congenital syphilis at the time of operation, and one has suffered two attacks of meningitis since operation.

Tinnitus was absent before and after operation in four cases and was not reported by three patients. Among the 70 remaining

cases tinnitus was absent after operation in 11 (16 per cent), reduced in intensity in 28 (40 per cent), unchanged in 20 (29 per cent) and made worse in 11 (16 per cent).

Hearing was abolished in all operated ears.

Tables II through VI are concerned with duration of disability after operation. In Table II, patients are grouped according to duration of symptoms prior to operation. It is seen that the duration of disability was least in those patients whose symptoms had been present less than one year and greatest in those whose symptoms had been present ten or more years. Results in patients whose symptoms had been present one to ten years approximated the mean. These data suggest that the duration of postoperative disability is influenced by duration of symptoms, possibly due to the nervous instability induced by the recurring episodes of vertigo.

TABLE II

RELATION OF POSTOPERATIVE DISABILITY TO DURATION OF SYMPTOMS PRIOR TO OPERATION (65 PATIENTS)

VERTIGO, YEARS	TOTAL PATIENTS	WORK DAYS LOST 1-30	31-60	61 days-4 mo.	5-12 mo.	< 60 days, % of patients
< 1	5	4	1	0	0	100
1- 2	18	5	6	4	3	61
3- 5	16	5	6	4	1	69
6- 9	6	3	3	0	0	100
10-14	11	4	2	2	3	55
15+	9	1	4	2	2	56

In Table III, patients are grouped according to age at time of operation. The majority of patients were in the fourth, fifth and sixth decades. The duration of disability was similar for all age groups except the group of persons 61 years old or older, who, contrary to our previous opinion, recovered more rapidly than younger patients. The shortest period of disability, seven days, was reported by a man aged 72 years.

TABLE III

RELATION OF AGE TO DURATION OF DISABILITY (65 PATIENTS)

AGE, YEARS	TOTAL PATIENTS	DURATION OF DISABILITY, DAYS 1-30	31-60	61 days-4 mo.	5-12 mo.	<60 days, % of patients
0-30	7	3	1	1	2	57
31-40	14	4	7	1	2	79
41-50	24	9	4	7	4	54
51-60	14	3	7	1	3	71
61+	6	3	3	0	0	100

TABLE IV

RELATION OF LABYRINTHINE FUNCTION OF OPERATED EAR TO DURATION OF DISABILITY (61 PATIENTS)

RESPONSE TO CALORIC STIMULATION	TOTAL PATIENTS	DURATION OF DISABILITY, DAYS 1-30	31-60	61 days-4 mo.	5-12 mo.	<60 days, % of patients
Absent	7	2	3	1	1	71
Hypoactive	43	16	13	8	6	67
Normal	10	2	5	1	2	70
Hyperactive	1	1	0	0	0	100

The relation of preoperative labyrinthine function to duration of disability is depicted in Tables IV, V and VI. Of the 77 patients studied, four did not have labyrinthine tests prior to operation, duration of disability is unknown in 11, and one patient submitted to bilateral labyrinthotomies. Data from the remaining 61 patients reveal that 42 (69 per cent) returned to full activity within 60 days following operation.

Table IV reveals that response to caloric stimulation was absent or hypoactive in 50 of 61 operated ears; in 34 of these (68 per cent) rehabilitation occurred within 60 days. Response to caloric stimulation was normal or hyperactive in 11 ears subjected to operation; duration of disability was less than 60 days in eight of these (73 per cent).

TABLE V

RELATION OF LABYRINTHINE FUNCTION OF UNOPERATED EAR TO DURATION OF DISABILITY (61 PATIENTS)

RESPONSE TO CALORIC STIMULATION	TOTAL PATIENTS	DURATION OF DISABILITY, DAYS 1-30	31-60	61 days-4 mo.	5-12 mo.	< 60 days, % of patients
Absent	1	1	0	0	0	100
Hypoactive	13	2	4	4	3	46
Normal	47	18	17	6	6	74
Hyperactive	0	0	0	0	0	0

TABLE VI

RELATION OF LABYRINTHINE FUNCTION OF BOTH EARS TO DURATION OF DISABILITY (61 PATIENTS)

RESPONSE TO CALORIC STIMULATION *Operated*	*Unoperated*	TOTAL PATIENTS	DURATION OF DISABILITY, DAYS 1-30	31-60	61-120	121+	< 60 days, % of patients
Absent	Absent	1	1	0	0	0	100
Absent	Hypoactive	2	0	0	1	1	0
Hypoactive	Hypoactive	11	2	4	3	2	55
Absent	Normal	4	1	3	0	0	100
Hypoactive	Normal	32	14	9	5	4	72
Normal	Normal	10	2	5	1	2	70
Hyperactive	Normal	1	1	0	0	[illegible]	100

Table V shows that response to caloric stimulation was absent or hypoactive in 14 unoperated ears; duration of disability was less than 60 days in seven of these (50 per cent). Labyrinthine response was normal in the unoperated ears of 47 patients; duration of disability was less than 60 days in 35 (74 per cent) of these patients.

Table VI classifies patients according to the response to caloric stimulation in both ears. The groups in this classification are small; however, in one of the two largest groups, rehabilitation occurred within 60 days in 72 per cent of patients in whom preoperative tests

TABLE VII

RELATION OF DURATION OF SYMPTOMS
TO POSTOPERATIVE EQUILIBRIUM

VERTIGO, YEARS	TOTAL PATIENTS	POSTOPERATIVE EQUILIBRIUM, CLASS I	II	III	IV
<1	6	2	2	2	0
1- 2	24	6	7	10	1
3- 5	17	4	8	4	1
6- 9	9	2	3	2	2
10-14	12	5	5	2	0
15+	9	3	2	4	0

TABLE VIII

RELATION OF AGE AT OPERATION
TO POSTOPERATIVE EQUILIBRIUM

AGE, YEARS	TOTAL PATIENTS	POSTOPERATIVE EQUILIBRIUM, CLASS I	II	III	IV
0-30	9	2	2	4	1
31-40	16	5	6	5	0
41-50	26	8	9	7	2
51-60	17	5	5	6	1
61+	9	2	5	2	0

showed reduced function in the operated labyrinth and normal function in the unoperated labyrinth, while in the other group the same result was achieved in only 55 per cent of patients in whom both labyrinths were hypoactive prior to operation. It is interesting to note that rehabilitation occurred within 30 days in both the patient who had no response from either labyrinth and the patient whose operated labyrinth gave a hyperactive response.

In this series of patients, response to caloric stimulation provided a poor index of rate of recovery; however, the function of the unoperated ear was slightly more reliable than that of the operated ear.

TABLE IX

RELATION OF PREOPERATIVE LABYRINTHINE FUNCTION TO POSTOPERATIVE EQUILIBRIUM (73 PATIENTS)

OPERATED EAR	TOTAL PATIENTS	POSTOPERATIVE EQUILIBRIUM, CLASS I	II	III	IV
0	7	2	2	3	0
–	55	16	20	15	4
+	10	3	5	2	0
++	1	0	0	1	0

TABLE X

RELATION OF PREOPERATIVE LABYRINTHINE FUNCTION TO POSTOPERATIVE EQUILIBRIUM (73 PATIENTS)

UNOPERATED EAR	TOTAL PATIENTS	POSTOPERATIVE EQUILIBRIUM, CLASS I	II	III	IV
0	1	0	0	1	0
–	18	4	8	3	3
+	54	17	19	17	1

The patient who underwent bilateral labyrinthotomies was a deaf mute aged 23 years whose preoperative labyrinthine responses were hypoactive in both ears, and who had experienced vertigo for 15 years. The patient returned to work as a clothes presser three months after operation.

Tables VII, VIII, IX and X depict respectively the influence of duration of symptoms, age, and response to caloric stimulation of the operated and unoperated ears on equilibrium following labyrinthotomy. Reference to the criteria for classification of postoperative equilibrium reveals that the distinction between classes II and III is slight and may depend more on the choice of words used by the patient than on any actual difference in function. In the four patients of class IV, persistent episodes of vertigo were not primarily the result of unilateral absence of labyrinthine function; hence these

TABLE XI

RELATION OF TYPE OF HEARING LOSS TO DURATION OF DISABILITY (65 PATIENTS)

PREOPERATIVE HEARING	TOTAL PATIENTS	DURATION OF DISABILITY, DAYS 1-30	31-60	61 days-4 mo.	5-12 mo.	< 60 days, % of patients
End-organ	48	18	16	6	8	71
Nerve	17	4	6	5	2	59

TABLE XII

RELATION OF TYPE OF HEARING LOSS TO POSTOPERATIVE EQUILIBRIUM

PREOPERATIVE HEARING	TOTAL PATIENTS	POSTOPERATIVE EQUILIBRIUM, CLASS I	II	III	IV
End-organ	58	17	19	18	4
Nerve	19	5	8	6	0

patients should not be considered in the evaluation of preoperative findings. Reference to the four tables reveals a striking uniformity in the distribution among classes I, II and III according to the various factors studied.

The hearing loss of Ménière's disease is characteristically of the end-organ type. In some cases of long-standing disease, changes characteristic of nerve dysfunction develop. Tables XI and XII reveal the duration of disability and the postoperative equilibrium associated with each type of hearing loss. The results do not vary significantly from the mean for all cases.

It is logical to anticipate that those patients who are able to return to full activity in a short period would also experience the greatest recovery of equilibrium. The data in Table XIII confirm this assumption. Complete restoration of equilibrium was experienced by 36 per cent of patients able to return to full activity within

TABLE XIII

RELATION OF DURATION OF DISABILITY TO POSTOPERATIVE EQUILIBRIUM

DISABILITY, DAYS	TOTAL PATIENTS	POSTOPERATIVE EQUILIBRIUM, CLASS I	II	III	IV
1-30	22	6	7	9	0
31-60	22	10	8	4	0
61 days-4 mo.	11	1	4	5	1
5-12 mo.	10	3	5	2	0
No report	12	2	3	4	3

60 days, and by 18 per cent of those whose period of disability was greater than 60 days.

COMMENT

The data elicited in this study do not support the findings of Day[2] and Cawthorne.[1] Return to full activity was achieved within 60 days by 68 per cent of patients in whom caloric tests indicated reduced function of the operated ear and by 73 per cent of patients in whom function of the unoperated ear was normal. Neither figure is significant when compared with the 69 per cent for the entire group who recovered within 60 days.

The other preoperative factors studied (age, duration of symptoms and type of hearing loss) were equally disappointing as an index for predicting either rate of recovery or degree of freedom from disturbed equilibrium. The only permissible conclusion is that study of this group of patients does not indicate a valid index for the prognosis of destructive labyrinthotomy.

The wide scattering of results exhibited within the several classifications studied suggests that the rate of recovery after unilateral labyrinthotomy depends more on factors such as nervous stability, ambition and economic necessity than it does on labyrinthine function, age or duration of symptoms.

The results suggest that the patient who plans destructive labyrinthotomy for the treatment of unilateral Ménière's disease may

anticipate relief from recurring episodes of severe vertigo. Two patients (3 per cent) suffered recurrence of episodic vertigo due to involvement of the unoperated ear following initial periods of relief. The patient may also anticipate return to his previous occupation although mild degrees of disequilibrium persisted in 71 per cent of the cases studied. We feel that the patient considering operation should be informed of the probability that he will not completely compensate for the loss of a labyrinth.

Destructive labyrinthotomy was done on the more severely affected ear of one patient known to have bilateral Ménière's disease. This patient also presented evidence of congenital syphilis, which had been treated intensively and was considered inactive by the syphilologist. The patient had not responded to medical therapy including streptomycin in doses of 6 gm daily. Following operation, symptoms referable to the unoperated ear were temporarily controlled by medical therapy. He was gainfully employed for a few months but has since been disabled by severe vertigo. This experience suggests that operation should not be done in cases of bilateral Ménière's disease.

The deaf mute patient who underwent bilateral labyrinthotomy was unable to work prior to operation. He has been self-supporting since three months after operation although he describes symptoms characteristic of complete absence of labyrinthine function. Bilateral operations are rarely justified.

Several surgical techniques were employed in this group of cases. The technique currently used includes avulsion of the membranous horizontal semicircular canal and insertion of bone chips into the fenestrated canal. Electrocoagulation was abandoned because of the occurrence of temporary paresis of the facial nerve in three cases. Occurrence of meningitis in two cases led to packing the canal with bone chips in an effort to secure solid closure of the canal. No effort is currently made to conserve hearing in the operated ear. Such efforts were unsuccessful in our hands, which confirms the opinion of Day.[4]

SUMMARY

Seventy-seven cases in which destructive labyrinthotomy was done for intractable Ménière's disease were studied. Seventy-three

patients returned to full activity. Continued disability was the direct result of operation in only one of the remaining four cases. Return to full activity occurred within 60 days in 69 per cent of cases. Mild disequilibrium persisted in 71 per cent. No criteria for prediction of duration of disability or freedom from disequilibrium were found. Total loss of hearing occurred in all operated ears. Tinnitus was relieved in 16 per cent, improved in 40 per cent, unchanged in 29 per cent and made worse in 16 per cent of cases.

MAYO CLINIC

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LIX

A MECHANO-ELECTRICAL THEORY OF COCHLEAR ACTION

HALLOWELL DAVIS, M.D.

ST. LOUIS, MO.

A major advance of the last few years in the physiology of the cochlea has been the description of various electrical potentials of the cochlea and the identification of the tissues that generate them. We can now combine this information with Békésy's description of the mechanical movements of the cochlear partition to give a theory of the mechano-electrical mechanism that excites the fibers of the auditory nerve. I shall summarize this theory and try to indicate the degree of certainty with which we infer the various relationships. To do this within the time available I shall assume that the traveling wave pattern of movement of the cochlear partition, so beautifully described and analyzed by Békésy[5], is familiar to all. The physical principles that underlie it seem to be established beyond any reasonable doubt.[3] Also well established is the duplex theory of hearing[9,17] which combines the place principle, i.e., a peripheral acoustic analyzer operating on the principles of resonance, with the frequency principle, i.e., the excitation of synchronized volleys of nerve impulses by transients and by individual sound waves of low frequency. Our interest today lies in the mechanism of stimulation of the nerve fibers.

The final step in this mechanism is still quite uncertain. The electric responses of the sensory cells may excite the nerve fibers directly or they may do so indirectly by governing the release of small doses of a chemical mediator such as acetylcholine. Our theory simply assumes that directly or indirectly the electric responses are an essential link in the chain of events. The circumstantial evidence for this assumption is very strong indeed although the proof is not yet absolute.

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ELECTRIC POTENTIALS OF THE COCHLEA

DC RESTING POLARIZATIONS
INTRACELLULAR: −50 TO −80 MV
HAIR CELLS, NEURONS, SUPPORTING CELLS, ETC
ENDOCOCHLEAR: +70 TO +85 MV
SCALA MEDIA ONLY

CM ALTERNATING CURRENT RESPONSE OF HAIR CELLS

SP DIRECT CURRENT RESPONSE OF HAIR CELLS

AP TRANSIENT RESPONSE : NERVE IMPULSES
IN NEURONS IN MODIOLUS

Fig. 1.

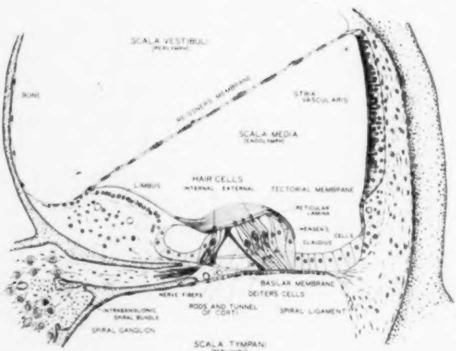

Fig. 2.—Cross section drawing of second turn of guinea-pig cochlea, based on a camera lucida tracing.[4]

There are four classes of electrical potentials of the cochlea. The first are the resting DC potentials which can be measured with micro-electrodes in the absence of acoustic stimulation. One of these is the familiar intracellular potential. All cells studied, including the nerve fibers, the hair cells, the supporting cells and the cells of the basilar membrane and Reissner's membrane, are internally polarized. Their interiors are 25 to 80 millivolts negative relative to the peri-

POTENTIALS IN FIRST TURN OF GUINEA PIG'S COCHLEA

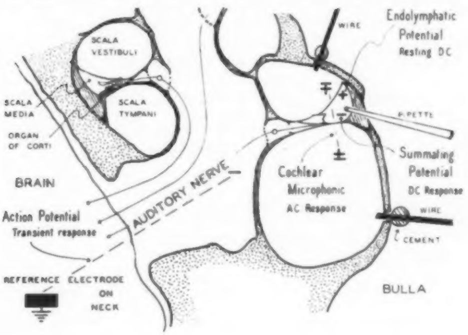

Fig. 3.—Diagram of electrode placements in the basal turn of guinea-pig showing also the location of the four potentials.[6]

lymph or the tissue fluids. The other is the positive "endocochlear" potential discovered by Békésy.[1] The endolymph is about 80 millivolts positive relative to the perilymph and the tissue fluids generally. Surprisingly, the endolymph of the saccule, the utricle and the semicircular canals do not share this strong positive polarization.

The source of the endocochlear potential has been identified beyond a doubt as the stria vascularis. Three groups of investigators, Tasaki, Misrahy, and ourselves, using three different methods, all agree on this point.[8,11,15] The most recent and elegant demonstration is the exploration by Tasaki with micro-electrodes under direct visual observation.

The mechanism of generation of the DC polarizations is unknown. We can only say that both the intracellular and the endolymphatic potentials depend more or less directly on oxidative metabolism. The two mechanisms differ in detail, however, and at present the endocochlear potential seems to be unique in electrophysiology. It may assist in giving the cochlea its extreme sensitivity but clearly the hair cells of the nonauditory labyrinth can function without it.

The action potentials of the auditory nerve are so well known and resemble those of all other sensory nerves so closely that they

DC POTENTIALS

INTRACELLULAR - NEGATIVE

ALL CELLS

IONIC CONCENTRATION: ONLY INDIRECTLY DEPENDENT ON OXIDATION

SOURCE OF ACTION POTENTIAL (NEURON)

PRIMARY SOURCE OF CM AND SP (HAIR CELL)

ENDOCOCHLEAR - POSITIVE

SCALA MEDIA ONLY : FROM STRIA VASCULARIS

DIRECTLY LINKED TO OXIDATION

SECONDARY SOURCE OF CM AND SP 1958

Fig. 4.

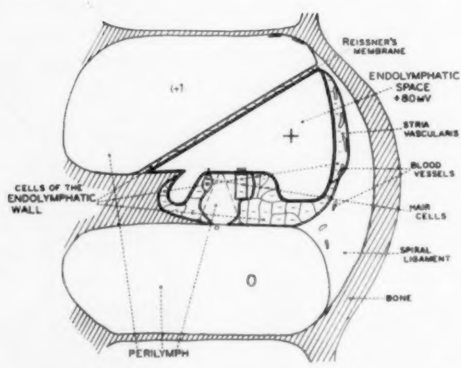

Fig. 5.—Diagram of the distribution of the DC potentials: intracellular (negative) and endocochlear (positive). Reference is perilymph of scala tympani.[16]

ENDOLYMPH

	COCHLEA	UTRICLE	SACCULE
DC POTENTIAL (MV.)	+ 65	+ 5	+ 2
POTASSIUM (M. EQ/L.)	138	141	-

Fig. 6.—Potential and potassium content of endolymph. These two features are not interdependent. The potassium concentration is about ten times that of perilymph: the sodium content is correspondingly lower. The high potassium content of fluid collected during measurement of the DC potential of utricle and scala media proved that the electrodes were actually in their intended positions.[14]

need only be mentioned in passing for completeness. They are part of the mechanism of conduction of the nerve impulses.

The cochlear microphonic (CM) is an alternating current response of the hair cells to acoustic stimulation. When the hair cells have degenerated, as from streptomycin poisoning, the cochlear microphonic is absent. Our recent experimental analysis,[8] using streptomycin and acute venous obstruction, shows that the cochlear microphonic is specifically the response of the external hair cells. If the internal hair cells remain the cochlear microphonic may be almost or completely absent, although nerve impulses may still be elicited by moderate and strong stimuli.

The electric response of the internal hair cells seems not to be a cochlear microphonic but to belong to the fourth class of cochlear potentials. These we have named the "summating potentials" (SP): they are DC responses to alternating acoustic pressure waves. The internal hair cell system apparently acts as a "detector" or "demodulator" and gives a DC response that increases with the root-mean-square acoustic pressure, integrated over one or two sound waves. The summating potential has been known for several years but has defied analysis until recently because of several puzzling and complicated properties. For example, although its usual direction is scala media (and vestibuli) negative relative to scala tympani it becomes positive under certain conditions, and with mild anoxia or other

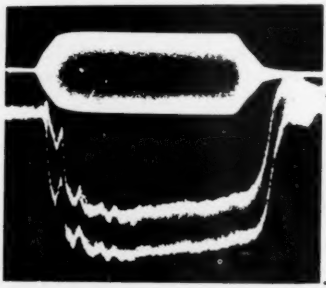

Fig. 7.—Action potentials, cochlear microphonics and summating potential recorded from the round window in response to a strong tone burst of 21.5 kc. Upper trace shows the time course of the stimulus. The slight rise in the base line during the tone burst in this and subsequent oscillograms is due to the condenser coupling of the amplifiers. (With a DC system the summating potential remains constant as long as the sound pressure level is unchanged.) In this and all subsequent oscillograms an upward deflection means scala vestibuli is more positive relative to scala tympani or else cochlea is more positive to neck. (Pestalozza, G., and H. Davis. Amer. J. Physiol. 185:595-600, 1956)[7]

injury (such as streptomycin, quinine, abnormal ionic concentrations, etc.) it increases instead of decreasing like the cochlear microphonic.[7,8]

The vagaries of the summating potential can be reconciled by the following theory. The cochlear microphonic and the summating potentials are all produced by the bending of (or a shearing action on) the hairs of the hair cells. The bending must be in the proper direction. For the external hair cells the direction is transverse to the long dimension of the organ of Corti. Bending the hairs outward makes scala media more negative. Bending inward makes it more positive. Bending lengthwise of the organ gives no effect. The critical direction for the inner hair cells is nearly parallel to the long dimension. Bending toward the apex makes scala media more negative. All of these directions have been established directly by Békésy with his vibrating micro-electrodes: they are not theoretical.[2] The mechanism by which the bending causes the electrical change is not known, but the energy is derived from the tissues of the cochlea, not from the acoustic signal. The piezo-electric theory, popular twenty years ago, cannot account for the amount of electrical energy

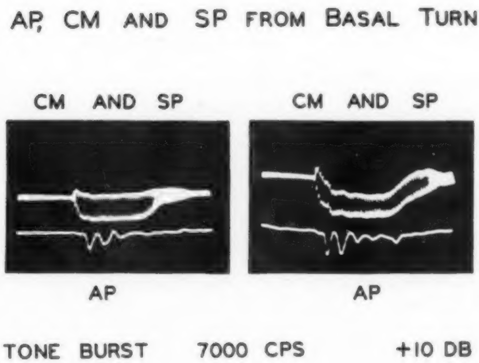

Fig. 8.—Cochlear microphonic and summating potential (upper traces) and action potential (lower traces) from basal turn in response to strong 7000 cps tone bursts. The duration of the plateau of the tone burst for this and most of the subsequent oscillograms was 4 msec. The rise time was always 1 msec. The AP trace shows successive volleys of synchronized nerve impulses following the onset of the tone burst. The stimulus was 10 db stronger for the responses on the right. SP is larger but CM is slightly smaller, although the CM response to the echoes is larger. The first stimulus was maximal for CM, the second was supramaximal.[7]

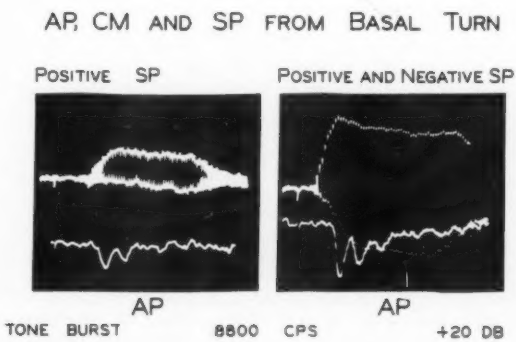

Fig. 9.—Left: a pure positive summating potential and CM in response to a weak 8800 cps tone burst. Such responses are exceptional. Right: the response to a stimulus 20 db stronger. Here the initial positive SP is soon overbalanced by a superimposed negative SP. Lower traces show AP.[7]

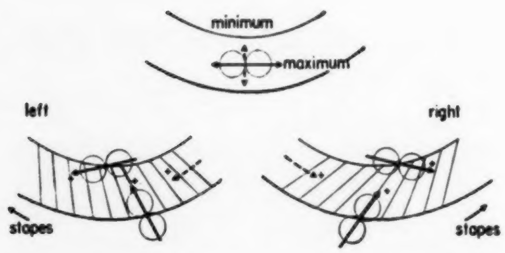

Fig. 10.—Directional sensitivity of the microphonics for a laterally vibrating needle on the outer, middle and inner edges of the tectorial membrane for both ears. The drawing is made by looking at the cochleas from the ventral side. The direction in which the stapes is located along the cochlear partition is marked. (From Békésy, G. v.: J. Acoust. Soc. Amer. 25:786-790, 1953.)

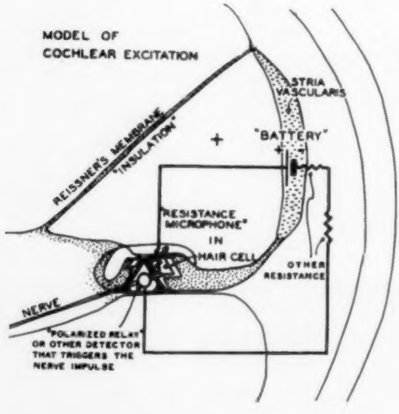

Fig. 11.—An electrical model of excitation of nerve impulses in the cochlea. Additional "batteries," not shown in the diagram, are located at the cell membranes of the hair cells and of the nerve endings. The return circuit from nerve ending to the stria vascularis is not restricted to the narrow anatomical path indicated in the diagram but is diffuse through all intervening tissues except the scala media.[6]

CM AND SP−

EXTERNAL VS INTERNAL HAIR CELLS

SIMILAR ELECTRIC RESPONSES TO BENDING OR SHEARING MOVEMENTS OF THE HAIRS

DIFFERENT MECHANICAL ACTION PRIOR TO BENDING THE HAIRS IS RESPONSIBLE FOR AC VS DC DIFFERENCE

SP+ IS LIKE SP− : BUT BENDING IS IN THE OPPOSITE DIRECTION

CM (E.H.C.) IS MORE SENSITIVE AND ALSO MORE VULNERABLE

1958

CM (E.H.C.) AND SP− (I.H.C.) MECHANISMS OVERLAP AT MEDIUM INTENSITIES

Fig. 12.

released by sustained displacements of the cochlear partition. Most probably the bending of the hairs "valves" electrical energy from the intracellular polarization of the hair cells and from the endocochlear potential (acting as two batteries in series) by changing the ohmic (DC) resistance across the hair-bearing surface of the hair cells.[6] Experimentally we have found that both CM and SP are increased or decreased, as would be expected on this theory, by artificially polarizing the cochlear partition positively or negatively with an additional external battery.[7]

A major feature of the theory is that the AC character of the cochlear microphonic on the one hand and the DC character of the summating potentials on the other are caused by differences in the mechanical events that determine the bending of the hairs. Otherwise the responses are similar; and when scala media becomes more negative the associated change in current flow tends to stimulate the nerve endings. (Actually it would be more accurate to say that the flow of current is the primary event and that it causes the scala media to become more negative.)

The transverse bending of the external hairs is assumed to occur according to the classical mechanical model. To account for the longitudinal bending of the inner hairs we must assume a longitudinal

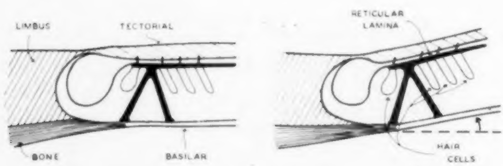

Fig. 13.—Diagrams to show how transverse bending of the basilar membrane causes radial bending of the hairs.

GENERATORS OF POTENTIALS

STRIA VASCULARIS		ENDOCOCHLEAR POTENTIAL	DC
EXTERNAL HAIR CELLS			
	PRIMARY RESPONSE	COCHLEAR MICROPHONIC	CM
	SECONDARY RESPONSE	POSITIVE SUMMATING	SP^{+}_{E}
	[SP- FROM E.H.C. NOT IDENTIFIED]		
INTERNAL HAIR CELLS			
	PRIMARY RESPONSE	NEGATIVE SUMMATING POTENTIAL	SP-
		CAN BE REVERSED MECHANICALLY	SP^{+}_{I}
	[CM FROM I.H.C. NOT IDENTIFIED]		1956

Fig. 14.

movement of tectorial membrane relative to the organ of Corti. The details are hypothetical, but the movement seems to be associated with the longitudinal traveling waves. In response to low frequencies the summating potential does not appear in the basal turn but only in the apical region where there are significant phase differences along the cochlear partition and where eddies tend to form in the cochlear fluids. The appearance of the eddies demonstrates qualitatively the presence of the necessary longitudinal forces.

It is significant that the threshold for detection of the negative summating potential is normally at least 20 db above that for the

FUNCTIONS OF COCHLEAR POTENTIALS

DC SENSITIZER OF HAIR CELLS : NOT ESSENTIAL

CM LOW LEVEL RESPONSE : E.H.C.

SP- HIGH LEVEL RESPONSE : I.H.C.

STIMULUS TO NERVE ENDINGS

SP+ FUNCTION UNKNOWN : E.H.C. AND I.H.C.

1958

AP ACTION POTENTIAL OF AUDITORY NERVE

Fig. 15.

cochlear microphonic. The external hair cell system which produces the latter is very sensitive, and also more vulnerable to injury. The inner hair cell system which produces the negative summating potential is less sensitive, more rugged, and continues to increase its output at high levels where the cochlear microphonic mechanism reaches a maximum output.

To explain the anomalies of the negative summating potential we now assume that the external hair cells normally produce a small positive summating potential that wholly or partly obscures the negative potential from the inner hair cells until the stimulus is fairly strong. We suppose that the cochlear partition vibrates across a mid-position or operating point that moves slightly toward scala media as the amplitude of vibration increases. This would shift the electrical baseline to the positive side. But if the more vulnerable external hair cells are injured this positive summating potential, as well as the cochlear microphonic, decrease somewhat and the negative summating potential of the inner hair cells is revealed in its full strength.

A mechanical bias of the cochlear partition toward scala vestibuli may be produced by increasing the hydrostatic pressure in scala tympani. This we do by injecting Ringer's solution into the basal turn with an outflow provided at the apex. Scala media now becomes less

positive. Also the summating potential in response to a tone burst becomes less negative and may actually reverse to a positive response. This is probably due to an exaggeration of the normal positive SP of the external hair cells, and perhaps also to a change in the direction of longitudinal movement at the internal hair cells, or both. Increased pressure in scala vestibuli, as produced by strong inward movement of the stapes, increases the resting polarization and also causes larger negative summating responses.

The entire mechanism of the cochlear partition and its sensory cells is obviously complicated, but from this analysis emerges a new concept. We have two significantly different sensory systems, side by side, the external hair cell system and the internal hair cell system. The former is more sensitive and also more vulnerable. The latter is a high-level response system, more rugged and less sensitive, but with a sharper localization of its zone of activity along the cochlea. The negative summating potential, it will be recalled, is only generated in the region of sharp longitudinal waves while the cochlear microphonic is generated by all of the cochlear partition that is moved at all. The inner hair cell system, the generator of the negative summating potential, thus appears better adapted for acoustic analysis by the place principle. Its relatively discrete innervation[10] also suggests better spatial discrimination by this system. The external hair cell system, on the other hand, responds with synchronized impulses in many fibers to every wave of low frequency sound. This is exactly what is required for a telephone, or frequency theory. The response to individual waves should also make possible finer discriminations of time differences.

The internal system seems analogous to the hair cell systems of the nonauditory labyrinth, whose cells the internal hair cells closely resemble in their ultrastructure as seen under the electron microscope.[12,13] The presence of these two systems of different sensitivity helps to explain the great dynamic range of the auditory mechanism.

818 S. Kingshighway

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LX

FUNCTIONAL CHANGES IN INNER EAR DEAFNESS

MERLE LAWRENCE, PH.D.
(By invitation)
ANN ARBOR, MICH.

The otologist is now well armored for attacks on afflictions of the middle ear, but he has very little hope to give a patient whose deafness is caused by damage to the inner ear. This provides a most challenging frontier for the investigator interested in the causes of deafness and in the discovery of means for its relief. But this is a challenge loaded with pitfalls and rugged heights to climb, for the region of interest lies in a most inaccessible portion of the mammalian body, and any methods yet devised to observe directly pathological conditions introduce, themselves, modifications that obscure the conditions it is desired to study. Much has been learned, however, concerning the locus of lesions caused by noxious agents and of the nature of the morphological changes produced within the inner ear as the result of toxic substances or systemic disturbances within the body. But these are all observations after the fact, and most needed to supplement them are sensitive measurements of function that reflect what have been called "reversible changes" so that the course of events can be quantitatively followed as various experimental conditions known to bring about inner ear deafness are manipulated. It is apparent from many studies that the cause of inner ear deafness is an alteration of the sensory cells' functional capacity, and if there is any hope at all of reversing this situation it must lie in the ability to detect these changes early enough to prevent permanent injury.

From the Physiological Acoustics Laboratory, Department of Otolaryngology and Institute of Industrial Health, School of Medicine, University of Michigan. This investigation was supported in part by the Research and Development Division, Office of The Surgeon General, Department of the Army, under Contract No. DA-49-007-MD-634 and by funds for research in Human Resources, University of Michigan.

Living tissues of the body do not always stay at the same functional level. There is a constant ebb and flow of ability to perform and this characteristic has been described as a continual interplay between life and death processes within the cells. Osterhout,[1] in a fascinating description of attempts to quantify these, describes injury to tissues as aiding, or hastening, the death process, and shows evidence that if the injurious condition persists the life process of the tissue reaches a point where no recovery is possible and viability is completely lost. If the disrupting factors are removed before this point is reached the tissues will, after a period of time, recover their normal functional capacity.

In Figure 1 a diagrammatic presentation of this cycle is shown. There is represented at the left-hand end of the saw-toothed curve the varying capacity to function as the life processes go on within the tissue. At a certain time some injuring condition arises and the functional capacity begins to fall, but upon restoration of the normal condition the tissue gradually recovers; the rate of this being determined by the extent of the injury and the nature of the environment in which the tissues must recover. If during the recovery process the injurious condition is again applied the recovery will be halted and functional capacity again go downhill. If any injury is severe enough or continued for a long enough period the ability of the tissue to carry out its normal functions is reduced to a level from which it cannot recover and death follows. From this point on there is no therapy except to find a substitute for the living cell, and in the tissues of the inner ear, the organ of Corti, this hope is considerably less than for some other organ as, for example, the kidney.

The majority of studies on inner ear deafness have been morphological ones on ears in which the injurious condition has been carried beyond the limit of reversibility. Such reports have been extremely valuable in pointing out what diseases have done damage to the sensory cells, but, short of preventing the occurrence of an injurious condition, the subtle changes in ability to function must be detected early if any chance of reversing the situation is to exist. This is, at this stage of understanding, equally true in experimental investigations. In the study of the limit of reversibility it is desirable to measure the functional capacity of the sensory cell so that interference

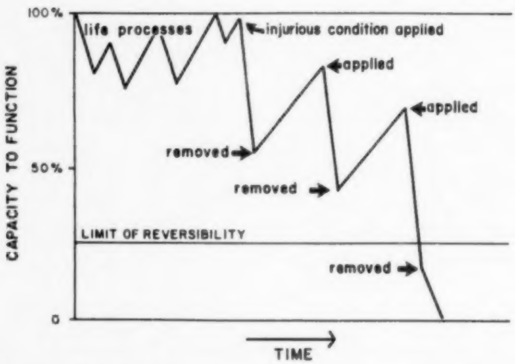

Fig. 1.—A schematic representation of the changes in the ability of a specialized cell system to function as some injurious condition is superimposed upon the normal life process of the tissue.

with the normal activities of this bridge between sound conduction and neural messages can be detected.

If we can imagine a bridge as somewhat analogous to the situation we might consider the function of the beautiful span over the Golden Gate in San Francisco to be that of delivering at one end those cars that entered at the other. Suppose that one day the normal number of cars are going onto the bridge (and let us assume only one-way traffic) but only about one-quarter of this number per hour are leaving, and let us suppose further that, except for the approach ramp, the bridge is not only invisible but inaccessible to the traffic analyzer. How could one find out what is wrong?

One could first examine the visible approaches only to find that nothing is amiss and that all the cars are proceeding as usual, disappearing into the invisible area. Next one might take air samples at various distances adjacent to the bridge in an attempt to pick up smoke or exhaust, but how discouraging this would be in the presence of other contaminants. Perhaps another method might be to place a stethoscope on some accessible portion of the bridge substructure, and send onto the bridge a test car while the observer listens to it rumble along, hoping to be able to determine whether something so

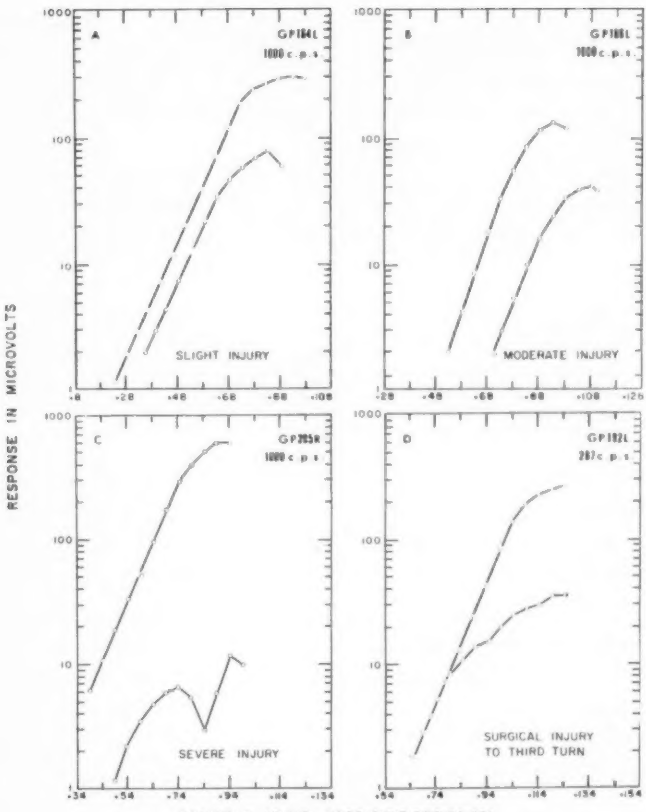

Fig. 2.—Pre- and postinjury intensity functions to show the shift in sensitivity, the increase or decrease in sound pressure needed to produce a maximum of response, and the change in the shape of the curve. A. A slight injury shows only a small shift of the function to the right but now a less intense sound is needed to elicit the maximum response. B. A moderate injury shifts the curve farther to the right and now a greater intensity is required to produce the maximum output. C. In severe injury the curve may take on a peculiar shape and show two or sometimes three separate rises. D. A surgical injury to the scala media of the third turn lowers the maximum but does not shift the curve at the low levels. Actually any one of these curves may be produced with any injury; they can only be determined by experiment.

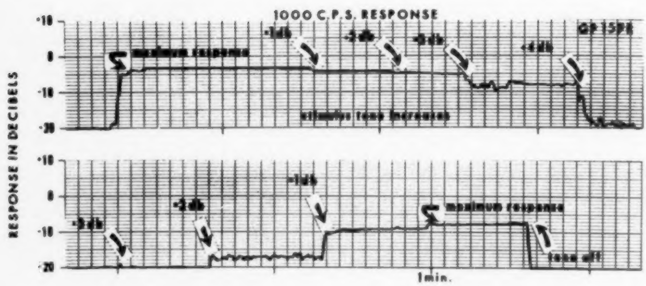

Fig. 3.—A running-time record of the response to 1000 cps as the sound is first increased by 1 db steps then decreased by the same amount. The increases of 1 db at the +3 db and +4 db points cause a sudden break in response. This ear has previously been overstimulated so that the maximum is down to 30 microvolts.

drastic has happened to the bridge that traffic is forever stopped, or whether by halting traffic for a period of time the situation might clear up. But care must be exercised to see that the test car is not the one to cause the final collapse of the bridge.

So it is with the ear; tests and visual observation may tell us the approach ramp to the inner ear is in good condition, but further examination tells us that of all the sound being sent in only a little, but some, is registered at the other end of the line. How to tell what has happened in between calls for experiment and our best experimental technique to date is to use the cochlear potentials as our stethoscope while sending in test tones under various conditions. The magnitude of the potentials in response to the test tone is the measure of the ability of these inner ear structures to function, and for the normal ear we know a great deal about the nature of this electrical response to tones of different intensities. As in the case of our bridge analogy, under normal traffic conditions, our stethoscope would reveal a steady rumble as the test car proceeds from one end to the other, and the more cars sent on, the greater the rumble. But what if something is wrong on the bridge? Will test cars merely give a diminished rumble or will something different be heard through the stethoscope? One thing is certain, the presence of a test car itself alters the conditions on the bridge.

Similarly, in studying the functional capacity of the ear we must determine the effects of the test tone itself. It has already been demonstrated that a test tone in an injured inner ear causes a further loss of function,[2-4] and that the more intense this test tone, the greater this additional loss. It is obvious that the intensity level of the test tone has a great deal to do with the function the tone is to measure. In fact this is true in the normal ear, for a tone that is too intense will produce inner ear damage. This is stimulation deafness and its immediate cause is damage to the sensory cells the same structure damaged in other conditions producing inner ear deafness.

It is essential then that the nature of stimulation deafness be understood both as to its onset in the normal ear and as a further insult to an already damaged ear. As long as this method of tapping in on the functional capacity of the sensory cells is employed in the study of the inner ear, the effects of the test tone itself must be recognized, and it has been the purpose of the experiments to be described here to study the nature of the cochlear response for different levels of intensity of stimulation before and after inner ear deafness has been produced. An additional purpose has been to demonstrate the injury-recovery cycle of the organ of Corti, and to determine the cumulative effects on a normal ear of repeating these measures.

EXPERIMENTAL RESULTS

The usual method of stimulating by means of a speaker unit mounted outside a sound-proof, shielded room and sound conducting tube to the animal's ear inside the room was employed.

Determination of the sound pressure was carried out by means of a calibrated WE 640AA condenser microphone-probe tube combination with the latter entering through the side of the sound conducting ear cannula and terminating concentrically with it. The cannula was tied into the external meatus of the animal so as to be as close to the tympanic membrane as possible thus forming a closed system between it and the diaphragm of the driver unit.

The cochlear potentials were recorded by means of a platinum-foil electrode placed on the round window membrane and an indiffer-

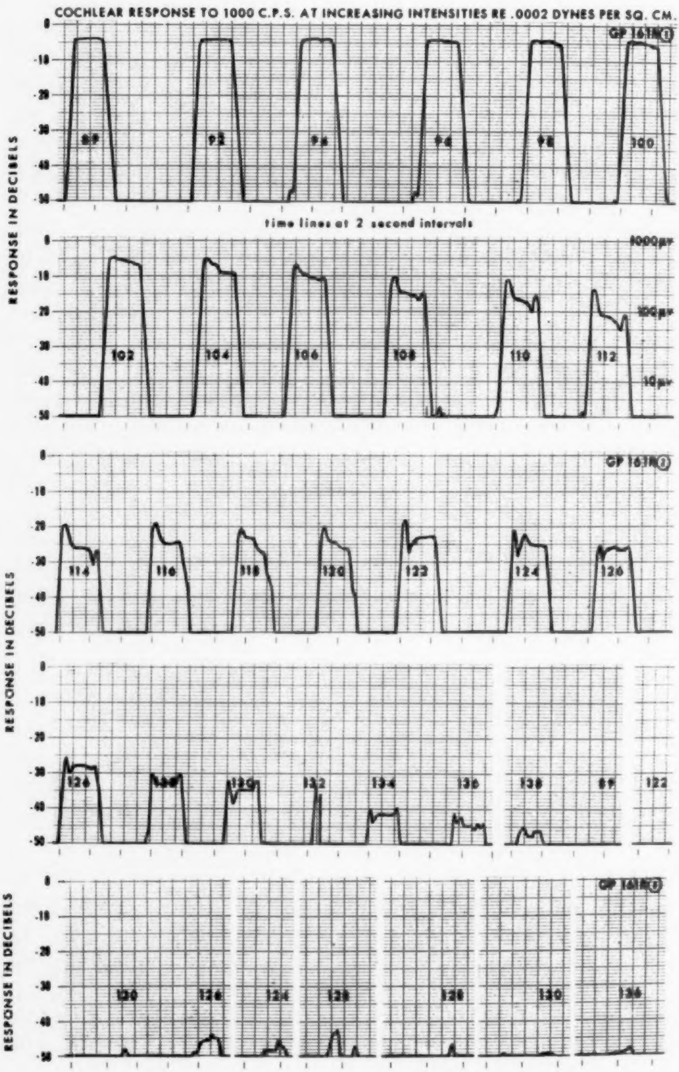

Fig. 4.—A sweep-amplitude record of the response to 1000 cps as the sound intensity is increased by 2 db steps for each presentation. The rise time is 1 second and the tone holds at its top intensity for one second. As the response gets increasingly smaller the actual sound is getting more and more intense which, in this case, has completely damaged the ear for this frequency.

ent electrode in the temporalis muscle. These responses were amplified 1000 times and read with a General Radio 736-A Wave Analyzer which serves to filter out nerve action potentials and other physiological noise.

The manner of tone presentation and method of recording were subsequently altered in ways to be described in order to determine various characteristics of the response.

The Shape of the Postinjury Intensity Function. The response of the ear to increasing intensities reveals the most information concerning the function of the sensory cells. As the level of the stimulus tone is increased the electrical response increases proportionally until a certain level is reached where this linear relationship ceases and the output increases by amounts that are only a portion of that of the stimulating tone. The response finally reaches a maximum and further small increases in stimulating tone produce only this same amount. Further increases in sound intensity produce a decrease in response and subsequently injure the sensory cells in which case the original curve may not be reproduced. Apparently, depending upon the severity of the injury, a great variation in this injury curve exists.

Figure 2 shows some of these variations. In (A) of the figure a slight overstimulation injury has produced a curve similar to the pre-injury one but shifted slightly to the right. It now takes a higher sound level to produce the same response provided the sound is kept in the linear region of the curve. The maximum is now not only lower but less sound intensity is required to produce it than before. In (B), from another animal and with a greater degree of injury than in (A), the injury curve is again shifted to the right but in this instance more sound is required to produce the maximum than before. After severe injury, as shown in (C), very odd-shaped postinjury curves may be produced. Here the response reaches a temporary maximum and then with further increases in sound begins to rise again. This may occur a third time, but, in any case, the test tone used to make these measurments produces further injury and with this technique it cannot be revealed whether the shape of the curve is a true measure of sensory cell function or is the result of introducing the test tone. The general characteristics of these postinjury functions as related to various overstimulating frequencies have been described elsewhere.[5]

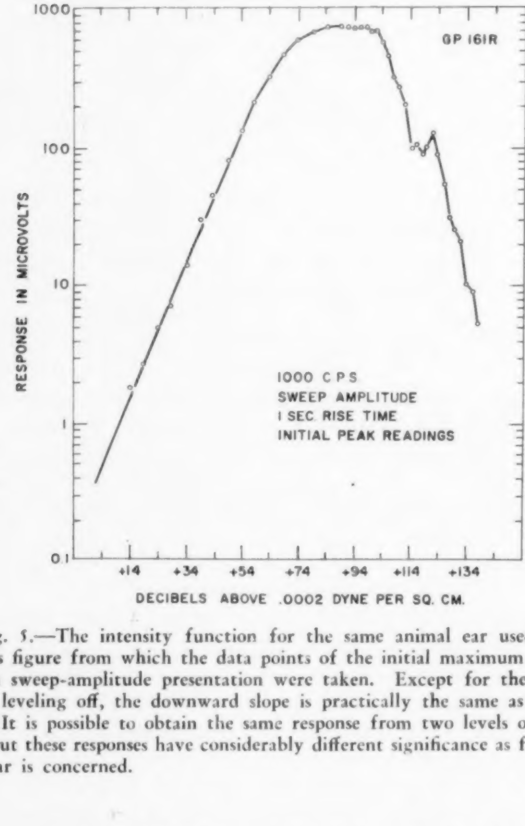

Fig. 5.—The intensity function for the same animal ear used in the previous figure from which the data points of the initial maximum response on each sweep-amplitude presentation were taken. Except for the characteristic leveling off, the downward slope is practically the same as the upward. It is possible to obtain the same response from two levels of stimulation but these responses have considerably different significance as far as the inner ear is concerned.

By introducing a needle into the scala media of the third turn so as to produce damage to the organ of Corti in that region the low-tone injury curve shown in (D) of Figure 2 was produced. Here at low levels there is no shift in sensitivity but the maximum is produced at a considerably lower response level.

Enough information is not yet at hand to enable us to predict what the shape of the injury curve will be, but it is obvious that any postinjury measure of functional capacity as reflected in the sensitivity of sensory cell response must be made with due considera-

tion of where on this response curve the measures are taken. But this, of course, still does not separate the effect of the test tone from the residual ability of the sensory cell to function.

The Onset of Injury. The eventual effect of a high-level test tone in a normal ear is to injure the sensory cells under test, while, with sensory cells that have been made more vulnerable by prior injury, the damaging effects of the test tone occur at lower response levels. When the maximum electrical output of the ear is reached it has been generally observed that the point of injury is being approached but the details have not been worked out even for the normal ear. In an injured ear the elicited response, if there is any at all, may be at the maximum-output level so the nature of the onset of injury becomes important.

In order to study the onset of injury it is necessary to use special recording techniques that will trace the response over a 60 db range for any period of time that the test tone may be presented. With the General Radio 736-A Wave Analyzer as the basic instrument the output of its variable-frequency oscillator was tapped and fed to a mixing circuit where it was combined with the output of a crystal-controlled oscillator of the same frequency as the crystal filters in the wave analyzer (approximately 50 kc). (Prof. Walter E. Rahm of Princeton University furnished the circuitry that made this procedure possible.) The higher combination tones were filtered out and the audio frequency (100 to 10,000 cps) fed to an electronic circuit that controlled the rate of rise of the tone, the extent of this rise, and the duration of the presentation. This was then amplified and fed to the speaker.

The potentials picked up at the round window were amplified and conducted to the input of the wave analyzer. This system then ties the sound source to the wave analyzer so that the six-cycle band width of the analyzer allows for the recording only of the tone presented. The 50 kc signal of the analyzer was amplified and fed to a Sound Apparatus Company Model SL-4 recorder with a 0-60 db input potentiometer.

Using this system of presentation and recording, the first experiment involved an ear whose response was previously depressed by overstimulation. The purpose was to determine the maximum and

subsequent reduction in response as the stimulating tone was increased. Shown in Figure 3 is the running-time record of the recorded potentials produced by a tone of 1000 cps at and above the region of maximum response which, in this instance, amounted to only 30 microvolts. As the tone is increased by one decibel steps beyond the maximum the level of response decreases by about the same amount until at +3 db there is a break and the response drops 5 db. Raising the sound level one more db to 4 db above that which gives the maximum produces a further drop of 12 db or a response 17 db below the maximum. Apparently the +1, +2 and +3 steps were not injury but represent a decrease in response because of the severe overloading of this partially damaged system.[6] At a rather specific point, however, further drastic injury occurs as evidenced by the sudden decrease in response and the failure of the maximum to be reproduced as the level of sound is decreased. As the tone is reduced 1 db at a time, as shown in the lower tracing of the figure, there is an increase in response which never reaches the previous level. The response to the second +3 db sound level is now down 11 db from the first +3 db reading; that of the +2 down 18 db from the previous and the +1 db and maximum down 5 db. It appears as if an overloading characteristic and an injury of about 5 db are combined at the +3 and +2 db stimulus levels; the end result obviously representing the influence of the test tone upon the residual capabilities of the inner ear.

If the tone is continually increased, the injury and overloading become more and more severe, and it is not possible to separate the two except by a recheck of the functional capacity at some low level of stimulation. Such a low level of stimulation is not possible if the injury is extreme and only a small response can be obtained. It is further obvious from the intensity functions of Figure 2 that the same magnitude of response can be obtained from two intensities of stimulation, one at a low level and one at a high level, and the two responses do not measure the same thing in connection with the functional capacity of the inner ear. The descending function of the cochlear response, which was not shown in the first experiment, is therefore of interest.

In determining the descending portion of the intensity function the effects of tone duration are minimized by employing very brief presentations. There is a cumulative effect of repeated presentations

so a continual running-time record has been kept, and Figure 4 presents the response to a 1000 cps tone as its amplitude is swept increasingly in steps of 2 db above the region of maximum response and held for about two seconds. At a sound pressure level of 89 db the response holds at a maximum of 630 microvolts. Increasing the intensity in the next presentation by 3 db does not change the level of response. When the sound is raised two more db, however, and held for two seconds there is seen a slight drop in response after the first second. As the tone is increased by 2 db steps the response goes up to a constant level but the immediate fall off becomes more noticeable until a sound intensity of 106 db is reached. Here is seen the first significant drop in the initial rise which now attains 450 microvolts. At 114 db the initial rise is 100 microvolts and the remaining portion shows a drop and secondary rise. At 120 db the initial rise improves a little but then the response slopes off rapidly while above this level there is a steady falling off of the initial rise with a decrease and second rise in the following two seconds. The response has dropped to a level of 10 microvolts when a sound pressure of 134 db has been reached and at 138 db only 5 microvolts can be attained. Repeating some of the earlier levels of stimulation now produces very little response; no potentials greater than 10 microvolts can be obtained with any level of sound. There is the question of whether the immediate fall off in response following the initial maximum can be accounted for by middle-ear muscle action. This remains to be studied more thoroughly, but there are some characteristics of the picture that mitigate a muscle action supposition: an animal immobilized by curare may show the same effects, and the fall off only occurs after the maximum has been reached. Also, the degree and maintenance of this decrease is variable in amount, being very little at first, becoming quite marked for higher stimulus intensities and finally, at the extremely high intensities, showing an initial drop, a leveling off and then a slight rise as the stimulus tone decreases. Regardless of what produces this drop there is no question that something happens to the response almost immediately after the tone is presented and reaches its maximum. For this reason then, in plotting the descending portion of the intensity function, only the initial peaks of response are used.

Figure 5 shows the complete intensity function for 1000 cps from the animal whose record has been discussed in connection with the previous figure. The linear, nonlinear, and maximum areas of

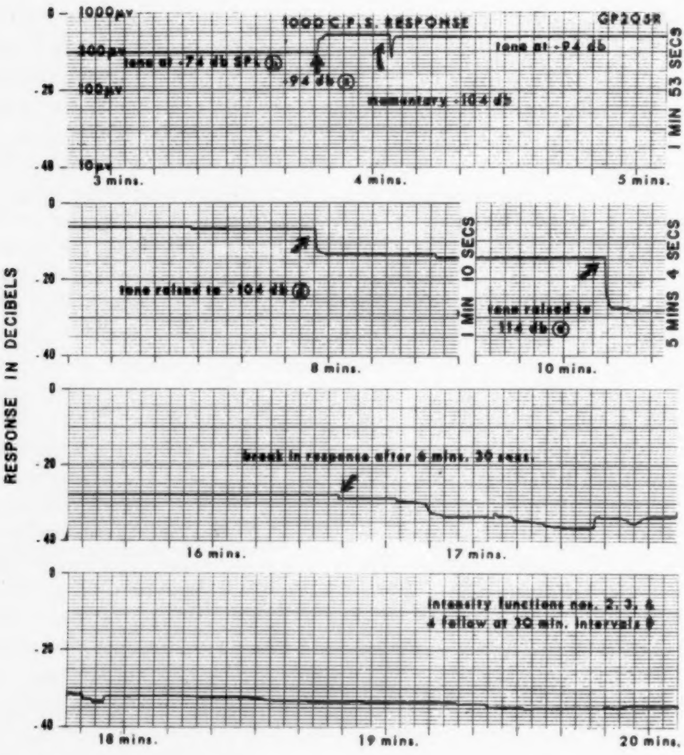

Fig. 6.—A running-time record of the response to 1000 cps as the stimulus at different levels is left on for a period of time. A break in the response comes after the tone at +114 db had been left on for six and one-half minutes. The letters in circles and sound pressures refer to the next figure.

response present the usual form and the descending portion, except for a slight rise at 100 microvolts, is almost of the same slope as the ascending portion but a little more erratic. The second rise is characteristic of this descending response and there is no immediate explanation for it; it seems to represent a moment of resistance for the inner ear and it may be related to the degree of permanent injury

that follows. The entire curve also clearly shows how two widely separate levels of stimulation can give rise to the same response; both a sound pressure level of 30 db and 134 db give a response of 10 microvolts.

One might ask why this is never noticed audiometrically; why, if, as is almost invariably the case in animal recording, the maximum of the cochlear response is reached at a sound pressure level of 90 db to 100 db, does loudness always continue to grow in human hearing as long as the tone is increased? In explanation of this it must be kept in mind that we are only recording the response to one tone, in this case 1000 cps, and that all of the harmonics that arise within the ear as the nonlinear portion of this response curve is traversed are filtered out. In listening, the fundamental and harmonics are all heard and the total combination adds to loudness. In animal experiments it has been shown that the harmonics rise regularly and rapidly, and when they are added to the fundamental the combined curve is practically linear.[7]

The data of Figure 4 from which Figure 5 was made shows that the duration of the stimulus is an important factor in bringing on the onset of injury. Referring again to Figure 4 it can be seen that at 89 db the maximum is maintained for the duration of the tone while at 104 db, even though the maximum level of response is attained on the initial rise of the tone, the response immediately begins to drop off. The next experiment was carried out to see if there would be a sudden breakdown of function for long lasting tones as demonstrated in Figure 3 for increasing levels.

Figure 6 shows the results of such an experiment using the same method of recording as that used to produce the results of Figure 3. First refer to Figure 7 which shows (curve 1) the normal intensity function for 1000 cps in this particular animal. It was found that the tone could be kept on at +58 db (point a on the curve) for a long period of time (apparently within the survival limits of the preparation) with no deterioration in the response which remains at 54 microvolts. Raising the tone to +74 db (point b on the curve) for a response of 300 microvolts gave the same result and here the running record of Figure 6 starts. After a brief period of time the tone was raised to +94 db (point c on the intensity function). Momentarily raising the sound level of the tone to +104 db caused a

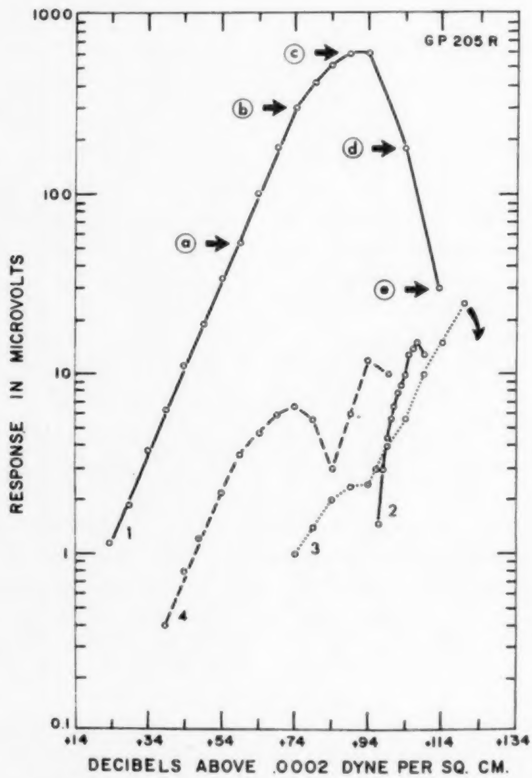

Fig. 7.—Intensity functions before and after various recovery periods following overstimulation. The letters on curve 1, the pre-injury function, refer to the stimulus shown in the previous figure which is for the same animal. Curve 2, 3 and 4 were made at 30 minute intervals following cessation of the record shown in Figure 6.

sharp drop so the tone was returned to +94 db and it can be seen that this brief stimulus brought on a slight drop in the maximum which now remains at 700 microvolts. Since the ear seemed to tolerate this level for a period of time with no loss, the tone was raised to +104 db. This level brought about a decrease in electrical output. Raising the stimulus level to +114 db (point c of Figure 7) dropped the response to 30 microvolts equivalent now to the maximum response of the animal shown in Figure 3. Maintaining this level of stimulation seemed to have no further effect until six and one-half minutes had passed at which time there appeared a sudden break in response. As shown in the recording, the response following this point became noticeably variable and continued to decrease somewhat until termination of the recording.

The data of Figures 3 and 6 show that what is probably a permanent loss of function comes on rather suddenly both with increasing stimulus level and with tone duration. In the introduction the concept of the limit of reversibility was discussed, and, if the sudden breaks in response brought on by intensity and duration represent severe injury, this rapid deterioration may be the passing of this limit for some sensory cells, in which case one might expect the inner ear as a whole would never return to its normal functional capacity. On the other hand the depression in response brought on by increasing intensities before the sudden break occurs may be the result of temporary injury which is reversible providing sufficient time in quiet is allowed for recovery. The two remaining experiments were carried out to test this.

The Recovery from Injury. The results shown in Figure 6 demonstrate the sudden injury break which is presumed to show the carrying of many sensory cells beyond the limit of reversibility on the injury-recovery cycle. As a measure of recovery further intensity functions were made after succcesive 30 minute intervals following the cessation of the Figure 6 record. These curves are shown as curves 2, 3 and 4 in Figure 7. There is recovery but it is incomplete, as predicted. It is not known, of course, whether there would have been complete recovery after a longer period of no stimulation, but previous experiments have demonstrated that this would probably not occur.[8] Of particular interest is the changing shape of the curves. Curve 2 shows a very rapid rise in response with small increases in stimulus intensity, but no responses at all are elicited for

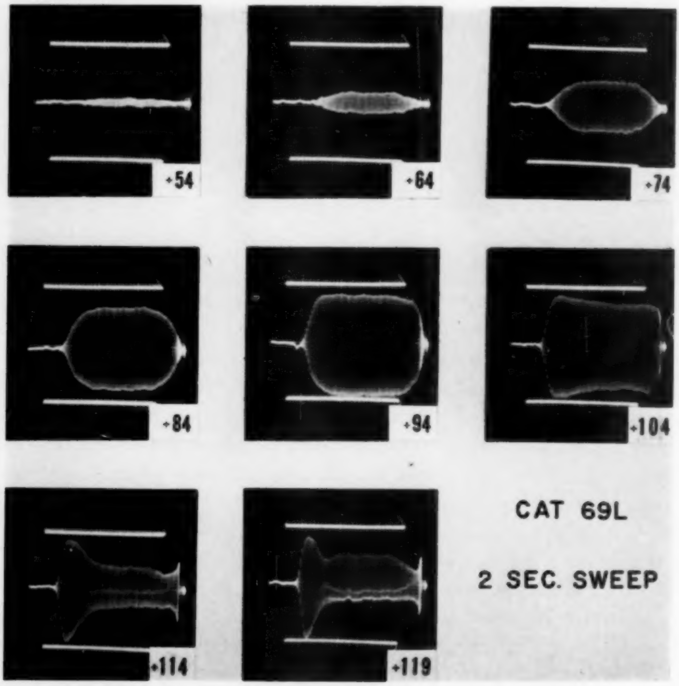

Fig. 8.—Sweep-amplitude records as shown on the cathode-ray oscilloscope for tones of increasing intensity. The immediate deterioration of the response following the initial peak is the same as the records shown in Figure 4. The fact that this only occurs after the maximum is reached and shows only a partial effect at first indicates inner-ear injury rather than muscle effect but this is not conclusive. The initial peaks only are used for plotting an injury-recovery curve.

sound levels which in the normal ear gave a maximum of 600 microvolts. Thirty minutes later some sensitivity has been regained at the low response levels but has been lost at the higher levels and the arrow pointing downward on the top of the curve indicates that a stimulus intensity of +119 db caused a sudden dropping of the response. During the next 30 minutes there seems to have been considerable recovery and sensitivity has been regained for all levels

of stimulation but the curve is now double, which is not uncommon for this kind of severe injury. Because of this peculiar characteristic there are now three levels of sound which will produce the same magnitude of response. This points out the importance of determining the entire function in making postinjury sensitivity measures in experimentally overstimulated animals.

The animal having been overstimulated by sound pressures lasting beyond the time necessary to produce the sudden break showed incomplete recovery. The further supposition has been that there is an injury and complete recovery cycle providing the sudden break point is not exceeded by either intensity or duration of stimulus. In order to measure this the tone was presented in sweep-amplitude fashion with fairly rapid rise times and the initial maximum of the response taken as the measure of functional capacity as was done for the animal shown in Figures 4 and 5. Because the response maximums did not show a loss with overstimulation in excess of 20 db and because the tone duration did not exceed two seconds it was possible to use the cathode-ray oscilloscope for making the determinations in order to take advantage of this instrument's rapid rise-time characteristics. Figure 8 shows the kind of readings that were made. These cathode-ray oscillographs represent the cochlear response for increasing intensities of tone as indicated. The white lines at top and bottom of each picture are calibrating lines representing 2828 microvolts peak-to-peak (1000 microvolts r.m.s.). When a stimulus level of +104 db is reached there is a maximum and then a gradual falling off. This is only a partial falling off of response and is not as severe as shown in successive increases to +114 and +119 db. Here again it is possible that this reflects middle-ear muscle activity but it should be kept in mind that it is not the characteristic picture of muscle activity. In each case the tone is still rising in intensity and does not start to decrease until after the maximum response has been reached, also distortion, indicated by the new line through the recording, increases at the moment of overall-response decrease. The same characteristic of the response is seen in the intensity function shown in Figure 5 and 7 as the stimulus tone increases beyond the maximum response. Our interest, however, lies in the maximum attained for each stimulus presentation. Figure 9 now shows the injury-recovery cycle made by such short sweep-amplitude measures before and following overstimulation. The first five points represent the maximum response attained before overstimulation. At point A a tone, at

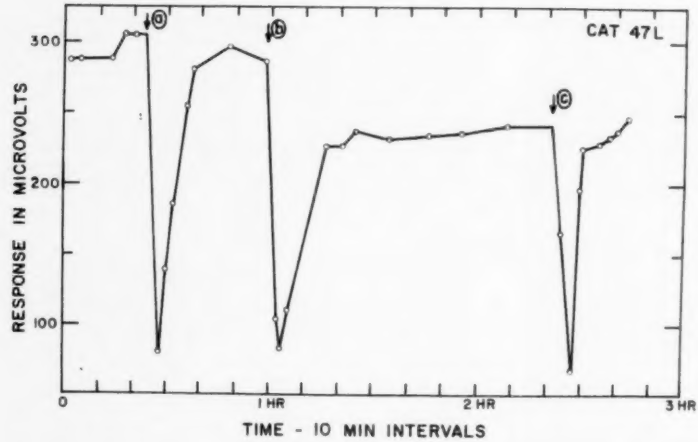

Fig. 9.—The injury-recovery curve as plotted from sweep-amplitude and cathode-ray oscillograph data. This appears very similar to the hypothetical curve of Figure 1.

a sound pressure level of +124 db, was presented for three minutes. This immediately dropped the response from 305 microvolts to 80 microvolts (11.6 db) but in a short time recovery is practically complete. At point B the same stimulus was again presented for three minutes and the drop in maximum response was the same. This time, however, recovery was not complete and the response returned only to 235 microvolts which is 2.3 db down from the normal maximum. A third period of overstimulation at the same intensity level but maintained only for one minute was presented at C, and this time the response returned to the second pre-stimulus level and appeared still to be recovering when the experiment was terminated. Even though the response returned to its normal level after the first stimulation, it would appear that some residual effect remained because the ear did not recover completely from a second overstimulation.

COMMENT

The organ of Corti is a delicate bodily tissue that survives through biochemical processes and responds to mechanical vibration

in such a way that the auditory nerve is stimulated and the sensation of hearing results. The secret of successful performance of this mission depends mainly upon the number, and roughly upon the location, of healthy sensory cells for which the rest of the organ serves as support. When something happens to injure these delicate cells such as their being deprived of nutritive material or poisoned by toxins, or when something disrupts the supporting structures, a loss of hearing results which can be detected audiometrically as inner ear deafness. At any moment during a cell's existence, as its metabolism changes in the course of normal life processes, a certain capacity to function exists, and when injury occurs it is superimposed upon the cell's momentary condition.[3,4] This decreases the functional capacity and when called upon to respond to a sound stimulus the performance of the organ of Corti is below normal which is reflected in a loss of hearing. Assuming that the sensory cells are like other specialized cells of the body in that they can recover from a temporary insult, providing it has not gone too far, the hope is that inner ear deafness can be reversed and normal hearing restored. This, of course, anticipates that means of counteracting or removing the injuring condition will be discovered. The problem raised here concerns the first steps in investigating the means for counteracting the now known factors that are injurious to the sensory cells.

Measuring the magnitude of the cochlear potentials arising from the inner ear when stimulated by sounds provides the best measure of sensory cell functional capacity, but this involves the introduction of test tones which must be raised to rather high levels when the organ of Corti is at a low ebb because of some previous injury. These high levels of test tone can cause further injury which changes the functional capacity of the cells under study. So the experiments here described have been devoted mainly to analyzing the factors of stimulation deafness related to the use of test tones following some previous injury to the inner ear. And for experimental purposes the ears were overstimulated to produce this injury.

Within the limits of this series of experiments it appears that the organ of Corti possesses a quantifiable ability to recover completely providing the injury has not exceeded a limit of reversibility. A ray of hope exists for the relief of inner ear deafness providing the loss in capacity to function along the injury-recovery-death cycle can be detected before the limit of reversibility is reached.

SUMMARY

These studies on the functional changes of the injured inner ear have shown the following:

1. When the ear is injured by overstimulation there is a point both for intensity and duration of tone where the response suddenly drops and presumably reflects irreparable damage of some sensory cells.

2. Following injury, the input-output function of the inner ear shows changes in shape, in slope, and in maximum output. When any measure of functional capacity is made on an injured inner ear the entire intensity function must be considered.

3. In order that the test tone might have a minimal influence on the ear under investigation the tone must be of short duration and controlled as to amplitude-sweep time and extent. If the tone is greater than that necessary to produce the maximum response there is an immediate fall off the extent of which increases with time and intensity level of the stimulating tone. It is not clear whether this is the result of middle-ear muscles exhibiting partial contraction or is an inner ear injury process. The present evidence favors the latter.

4. The inner ear can recover completely from an overstimulation injury providing this is not too great and that in experimental situations the tones used to test the inner-ear function are controlled so as to have a minimal effect themselves.

4506 Kresge Medical Research Building

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LXI

OBSERVATIONS ON TEMPORARY AUDITORY THRESHOLD SHIFT RESULTING FROM NOISE-EXPOSURE

Aram Glorig, M.D.

Anne Summerfield, Ph.D.

(By invitation)

W. Dixon Ward, Ph.D.*

(By invitation)

Los Angeles, Calif.

I

The Research Center of the Subcommittee on Noise has undertaken an extensive study of the temporary auditory threshold shift (TTS) produced by short exposures, eight hours or less, to various types of noise. One goal of the study is to determine the feasibility of using temporary threshold shift data to predict the amount of permanent hearing loss that will result from years of exposure to any given noise. Of interest also is the possibility of using some type of numerical correction to obtain valid estimates of resting thresholds from industrial audiograms known to be contaminated with TTS. The use of such a correction is dependent on our ability to predict with reasonable accuracy how much TTS will be present under any given conditions of noise-exposure. The studies reported in this paper are a first step in the collection of data that eventually will allow us to make such predictions.

There are many other uses to which our knowledge of temporary threshold shift can be put. We believe that if a noise does not produce a temporary hearing loss in one work day of exposure, it will

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* Research Center Subcommittee on Noise

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not produce a permanent hearing loss even after many years of exposure. If this is correct, temporary threshold shift can be used both to assess noise-exposures and to evaluate the effectiveness of ear protection. We hope eventually to be able to evaluate the significanc of individual differences in TTS including the effect of any existing permanent hearing loss on the further progress of loss. Finally, we expect to learn much about auditory physiology from comparisons of the behavior of TTS under many and varied exposure conditions.

THE PILOT EXPERIMENT

A five year laboratory study of temporary threshold shift was initiated with a pilot study. This study was designed to determine the general characteristics of the temporary threshold shift produced under rigidly controlled conditions of exposure and measurement and to determine the general feasibility of a long term study in terms of the reliability of equipment performance, subject performance, etc.

The main goals of the pilot experiment were:

1. To determine the course of temporary threshold shift growth and recovery for specified exposure conditions.

2. To determine the consistency with which the average temporary threshold shift of a group of subjects can be duplicated under the same noise-exposure conditions.

3. To determine the consistency with which the temporary threshold shifts of individuals can be duplicated under the same noise-exposure conditions.

4. To determine in part, by serial order of ear and frequency presentation, the effects of short time recovery on the threshold shift.

5. To determine, in part, whether shifts at any one frequency are highly related to shifts at other frequencies.

APPARATUS

Noise Source and Exposure Room. Thermal noise was fed through appropriate filter and amplifier circuits into an Altec Voice-of-the-Theater speaker. This speaker was located in a room that

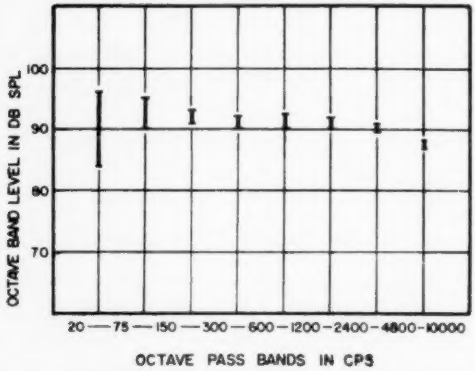

Fig. 1.—Range of sound pressure levels measured at six points in the unoccupied exposure room.

had plaster walls and a concrete floor and was reverberant. Variations in octave band levels of the exposure noise measured at six different points in the unoccupied exposure room are reported in Figure 1. The exposure field in the unoccupied room is uniform within plus or minus 1 db above 300 cps. Figure 2 shows the octave band levels measured at one point a) in the empty room and b) in the room occupied by six persons. Levels varied less than plus or minus 1 db with 0 to 6 persons in the room. Throughout the pilot experiment the over-all level of the exposure noise was maintained within plus or minus 1 db of 100 db re 0.0002 dynes per square centimeter. This level was monitored continuously during exposure.

Hearing Test Equipment. A modified Rudmose Bekesy-type automatic audiometer was used to measure the subjects' thresholds. Pulsed tones 1/4th second in duration were fed through the attenuator of the audiometer. Subjects were tested in a sound treated booth. PDR 8 earphones were worn.

EXPERIMENTAL PROCEDURE

Subject Orientation. Some 99 normal hearing persons participated in the study. Subjects were called to the laboratory for an

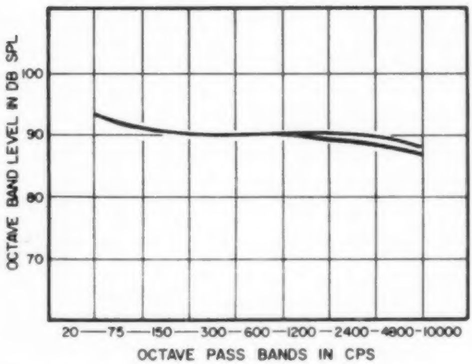

Fig. 2.—Octave band levels of noise in unoccupied exposure room (top curve) and in room occupied by six persons (bottom curve).

orientation session preparatory to the later noise-exposure sessions. The purpose of the orientation was 1) to give us an opportunity to make a manual audiogram for each participant, 2) to train subjects to place earphones properly (subjects put the earphones on themselves thereby conserving time by relieving the operator of the need to enter and leave the booth every time a subject entered for testing), and 3) to give subjects experience with the automatic audiometric equipment which they would use later.

Before each exposure-recovery test run, subjects were given an automatic audiogram on each ear at the frequencies included in the original manual audiogram. In addition, a threshold measurement was made of the particular frequency pair assigned to that subject. On the day of run number 1, subjects were assembled in a group for repeat instructions just before the exposure-recovery sequence was started.

Noise-Exposure. Subjects were introduced into the noise room one by one at three minute intervals. They read, studied, conversed, played checkers or chess, or filled out an MMPI score sheet, but were not allowed to sleep at any time during the noise-exposure (or recovery period). Subjects were encouraged to change places in the room

TABLE I

TIME PROCEDURE FOR A SINGLE MEASUREMENT FOR A SINGLE SUBJECT, WHO STARTED THE SEQUENCE ON HIS *RIGHT* EAR AND WHOSE FREQUENCY-PAIR WAS 3000 AND 4000 CPS

ELAPSED TIME	SUBJECT ACTIVITY	CARD	TRACE
0-28.7 seconds ↓	Enters booth, puts on and adjusts phones	3 KC	Set for Right Ear
61.1 seconds ↓	Completes trace	Same	Marked R_1 Switched to Left Ear
90.6 seconds ↓	Completes trace	Same	
97.3 seconds ↓	Waits for frequency and card change	4 KC	Set for Right Ear
129.9 seconds ↓	Completes trace	Same	Marked R_2 Switched to Left Ear
163.2 seconds ↓	Completes trace	Same	
184.0 seconds	Returns to noise room		

from time to time during exposure to minimize possible effects of slight differences in sound pressure level.

All exposures in this experiment were to wide band noise at 100 db re 0.0002 dynes per square centimeter. The total elapsed time of exposure for each run was two hours except for a) one group exposed for one hour only, b) one group exposed for six hours, c) a control group that had no noise-exposure.

Schedule of Hearing Measurements. Subjects in the two-hour group were tested after each 30 minutes of exposure. During each run the subjects received a total dose of two hours of noise-exposure interrupted by three three-minute test periods spaced at 30-minute intervals. A fourth hearing test was made at the end of the exposure period. The typical time schedule for hearing tests is given in Table I. During the two-hour recovery period, subjects were called to the test booths for threshold measurements at 30-minute intervals. The control group was run through the same test procedures as the two-hour exposure groups, but without noise-exposure.

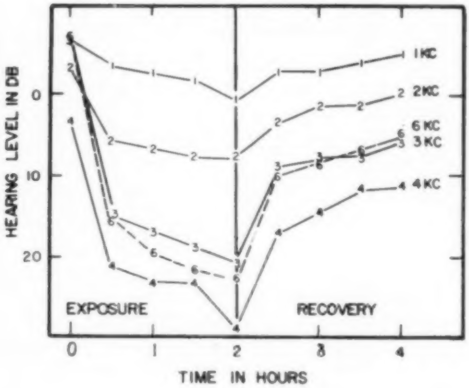

Fig. 3.—Course of growth and recovery of temporary threshold shift produced by exposure to continuous broad band noise at 100 db over-all sound pressure level.

Frequency and Test Order. The frequencies chosen for study were 1000, 2000, 3000, 4000 and 6000 cps but subjects were not tested at all frequencies. To maximize the amount of information that could be collected by testing more than one frequency in each person and by testing both ears on the same person, we tested at two frequencies in all subjects but kept each of the five test frequencies first in order of test for some subjects. A counter-balanced frequency presentation in five sub-groups of the total sample was made. One sub-group was tested at 3000 cycles first and 4000 cycles second. Another was tested at 4000 cycles first and 6000 cycles second, etc.

Replications. The two-hour exposure groups and the control group were run through the exposure-recovery test cycle on each of three different days. The one-hour and six-hour exposure groups were run through the exposure-recovery cycle on one day only.

RESULTS

Data from the pilot study have been analyzed in terms both of thresholds and of threshold shifts. Threshold shifts are reported here: first, because the scale starts at the same point for each fre-

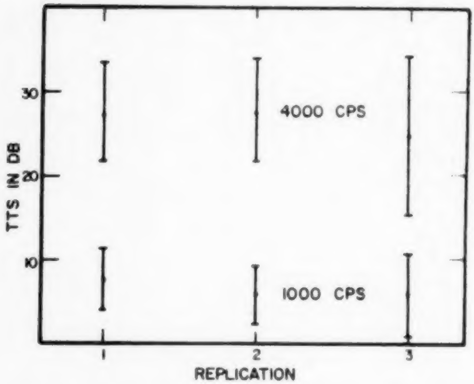

Fig. 4.—Mean temporary threshold shifts at 1000 and 4000 cps produced on each of three different days by two hours of exposure to broad band noise at 100 db. The vertical lines represent ± 1 standard deviation of the individual shifts from the group mean.

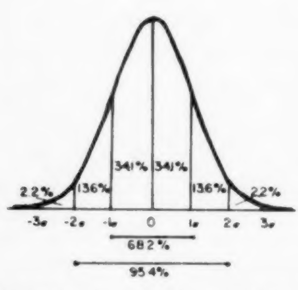

Fig. 5.—Normal distribution curve showing that 1) 68 per cent of the measurements of a normally distributed quantity fall within the range of values from the mean − 1 standard deviation to the mean + 1 standard deviation and 2) 95 per cent lie within the range mean ± 2 standard deviations.

TABLE II

EQUATIONS OF GROWTH AND RECOVERY OF TTS PRODUCED BY CONTINUOUS EXPOSURE TO BROAD BAND NOISE AT 100 DB

TTS	=	6.9	log Exposure Time	−	8.3	(1000 cps)
TTS	=	6.9	log Exposure Time	−	2.5	(2000 cps)
TTS	=	12.2	log Exposure Time	+	1.0	(3000 cps)
TTS	=	13.2	log Exposure Time	−	1.4	(4000 cps)
TTS	=	12.6	log Exposure Time	+	3.0	(6000 cps)
TTS	=	−3.3	log Recovery Time	+	8.7	(1000 cps)
TTS	=	−3.9	log Recovery Time	+	11.6	(2000 cps)
TTS	=	−7.3	log Recovery Time	+	24.4	(3000 cps)
TTS	=	−9.2	log Recovery Time	+	28.2	(4000 cps)
TTS	=	−8.7	log Recovery Time	+	30.9	(6000 cps)

quency, namely, zero shift, and thus the meaning of the quantities reported are more nearly comparable from frequency to frequency, and second, because there is a statistical advantage to the use of shifts. The distribution of thresholds is skewed but the distribution of the shift quantity is normal, thus allowing the use of means and standard deviations, etc.

Course of Growth and Recovery. Figure 3 shows a plot of mean temporary threshold shift as a function of time and of frequency for the two-hour exposure group. These curves represent mean shifts at the first frequency presented to the first ear tested. The initial rate of change of the shift is rapid; more than half the temporary threshold shift at all frequencies occurs within the first half hour of exposure. The magnitude of the maximum threshold shift varies with frequency, larger shifts occurring at the higher frequencies. The threshold changes are of the same general form at all frequencies.

These threshold shift values are best fit (by least squares fitting techniques) by a simple logarithmic function of time. The general form of the function is

$$\text{TTS} = \text{Const}_1 \log \begin{matrix}(\text{exposure}) \\ (\text{recovery})\end{matrix} \text{ time} + \text{Const}_2$$

Value of Const_1 and Const_2 are of the order of a few decibels. The specific formulas for each frequency are given in Table II.

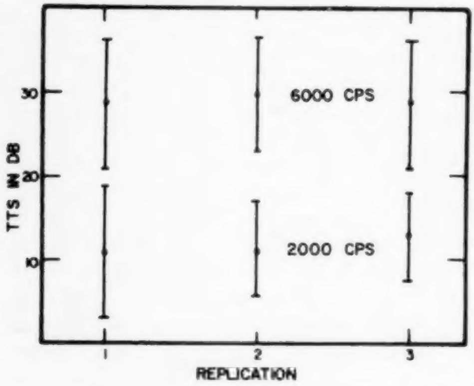

Fig. 6.—Mean temporary threshold shifts at 2000 and 6000 cps produced on each of three different days by two hours of exposure to broad band noise at 100 db. The vertical lines represent ± 1 standard deviation of the individual shifts from the group mean.

It now appears feasible to derive the constants in this equation empirically for any particular industrial noise situation and then to use the equation for estimating the possible variability in industrial audiograms due to the temporary threshold shift that occurs during a given work day. This procedure will be generally useful only if the logarithmic relation holds for types of noise other than the continuous noise used in our experiment, and then only if the short time recovery factors occurring under industrial test conditions do not significantly affect the threshold.

Repeat Consistency of Group Shifts. No statistically significant differences were found between the group two-hour shifts measured at each of the replications. Figure 4 shows the mean shifts at 1000 cps and at 4000 cps for each replication. These data represent only the first frequency presented to the first ear tested. The vertical lines which extend above and below the points in this figure are a measure of the spread of the individual shifts from which the average is calculated. These lines extend one standard deviation on either side of the mean. For the benefit of those persons who are not familiar with statistical terminology Figure 5 shows the curve typical of a normally

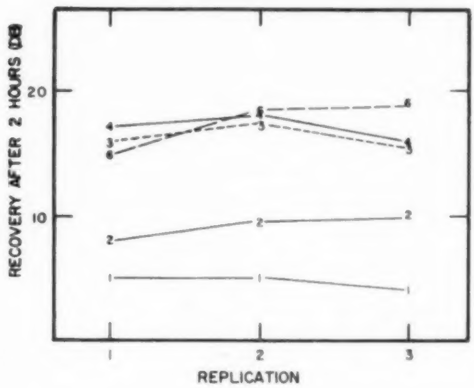

Fig. 7.—Mean temporary threshold shifts still remaining after two hours of recovery from two hours of exposure to broad band noise at 100 db. Mean shifts at 1, 2, 3, 4 and 6 kilocycles are reported for each of three replications of the exposure-recovery cycle. A different group of subjects is represented by each of the five frequencies.

distributed quantity. Numbers on the horizontal axis represent the measured values of the quantity, here the measured values of temporary threshold shift. Numbers on the vertical axis represent the portion of the sample studied that had a temporary shift of a given magnitude. The mean value of the shift quantity occurs at the peak of this curve. The vertical lines immediately to the right and to the left of the mean value have been drawn at the mean plus one standard deviation and at the mean minus one standard deviation respectively. As the numbers on this figure indicate, some 68 per cent or two-thirds of all the measured values lie between the number which is equal to the mean minus one standard deviation and the number which is equal to the mean plus one standard deviation.

To return to Figure 4, we see that the vertical lines drawn through the points represent the range of values which includes 68 per cent of the individual temporary threshold shifts. If these lines were extended to plus or minus two standard deviations around the mean, they would represent the range that includes more than 90 per cent of the measured individual shifts.

TABLE III

CORRELATION COEFFICIENTS OF TTS's PRODUCED IN SUBJECTS ON THREE DIFFERENT DAYS. EACH EXPOSURE WAS TWO HOURS OF CONTINUOUS BROAD BAND NOISE AT 100 DB

TWO HOUR SHIFT

FREQUENCY AT WHICH SHIFT IS MEASURED	CORRELATION OF SHIFTS AT 1ST & 2ND, 2ND & 3RD, AND 1ST & 3RD REPLICATIONS		
	r_{12}	r_{23}	r_{13}
1000 cps	.44	.47	.57
2000 cps	.66	.74	.61
3000 cps	.69	.95	.59
4000 cps	.52	.54	.49
6000 cps	.58	.68	.52

Figure 6 shows the mean and plus or minus one standard deviation about the mean for the temporary threshold shifts at 2000 cps and at 6000 cps. The magnitudes of the shifts at 3000 cps are approximately the same as those at 4000 and 6000 cps.

Figure 7 shows the magnitude of the average or mean temporary shifts still remaining at the end of the two-hour recovery period for each replication. To repeat, no statistically significant differences were found between mean two-hour shifts from any of the replications.

Repeat Consistency of Individual Shifts. Another question of importance to be answered from the replications is "To what degree is a person's threshold shift on one occasion predictable from his previous threshold shift under the same conditions?" Such consistency of individual shifts was evaluated by correlation procedures. The correlation of the subject's two-hour shift at each replication with that shift at each other replication for the first-ear-first-frequency tested is shown in Table III.

Temporary shifts of a group of ten subjects are included in each calculation. We feel that the consistency of the individual shifts is

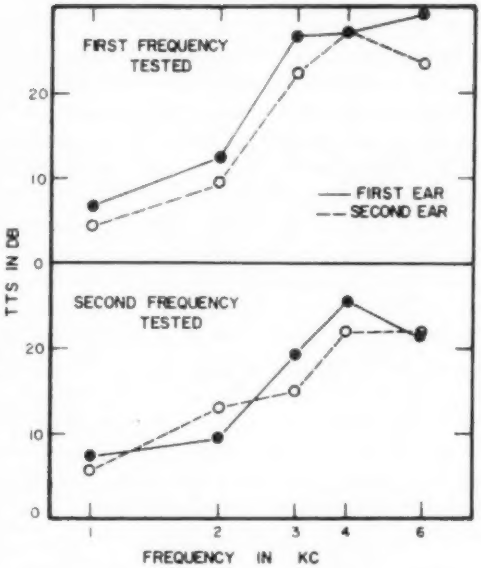

Fig. 8.—Effects of short time recovery on TTS at 1, 2, 3, 4 and 6 kilocycles. The top curves show the differences in TTS's at the first frequency presented to first ear tested (solid line) and TTS's at the same frequency tested about one minute later in the other ear (dotted line). The lower curves show the mean TTS's at second frequency tested in each ear.

high enough to justify further extensive investigation into the nature of temporary threshold shift.

An examination of the interrelations between within-day threshold shifts and between-day threshold shifts for the subjects in the control group indicates that practice effects did not noticeably affect the results of the pilot study.

Effects of Short Time Recovery. Subjects required approximately one-half minute to leave the noise and settle down to their first frequency check. The ensuing audiometric test period included four successive threshold measurements each taking about one-half minute to complete. It was possible that effects of very short term

recovery might be noticeable among the four successive threshold measurements. That some short term recovery occurred is evident from Figure 8. Compare the average two-hour shifts at each frequency measured at two different times: namely, in the ear tested first and approximately one minute later in the ear tested second. The top curves show the shifts at the first frequency tested, a) in the first ear and b) in the second ear. At all frequencies except 4000 cps, for the first frequency tested, the second ear shows less shift than does the first ear. A possible explanation is that sufficient short term recovery has occurred to be noticeable. Several analyses of variance were performed to test the statistical significance of these small differences. For 1000 cps and 3000 cps, whether they were tested first or second, there are significant differences between shifts in the first ear tested and in the second ear tested. At 4000 cps, there are no differences apparent. At 2000 cps and 6000 cps, there are significant reversals from first frequency tested to second frequency tested. These reversals may be explained by the fact that each point represents a different group of ears tested. The net result of these tests, however, is a strong suggestion that significant recovery occurs in the first few minutes; at least at all frequencies except 4000 cps.

CONCLUSIONS

The main conclusions to be drawn from the results of this pilot study are that the temporary threshold shift is a stable phenomenon and that a long term program of research into the nature of TTS and its relations to permanent hearing loss is entirely feasible. Specifically the results of the study show:

1. The temporary threshold shift (TTS) found under rigidly controlled conditions of noise-exposure and hearing measurement is a consistent repeatable phenomenon.

2. There are wide individual variations in amount of TTS produced by a given noise-exposure. These individual shifts are distributed according to a normal statistical distribution. Few persons have very large or very small shifts; the majority cluster about the average value.

3. The TTS produced by exposure to broadband noise of 100 decibels over-all level increases linearly with the logarithm of the exposure time at frequencies tested from 1000 cps to 6000 cps.

RESUMÉ

In this pilot study of temporary threshold shift (TTS) 99 normal hearing subjects were exposed to a laboratory-tailored, free-field, broad-band noise at 100 db SPL. Growth of and recovery from TTS were determined from auditory thresholds measured at 30 minute intervals during two hours of exposure and two hours of recovery immediately following the exposure. To allow estimates of repeat reliability of group shifts and of individual shifts each subject underwent the exposure-recovery test series on each of three different days. In addition, a control group of ten normal hearing subjects was run through the complete test procedure but without noise-exposure.

At all frequencies tested (1000, 2000, 3000, 4000 and 6000 cps) the growth and recovery of the temporary shift are logarithmic functions of time of the general form

$$\text{TTS} = \text{Const.} \times \log \text{exposure (or recovery) time} + \text{Const.}$$

The magnitude of the shift is larger at the higher frequencies. There is no consistent change in the magnitude of the two-hour shift from replication to replication either for the group mean shift or for individual shifts. There is no systematic change with replication in pre-exposure thresholds. Control group data indicate that practice effects did not influence the results.

111 North Bonnie Brae St.

OBSERVATIONS ON TEMPORARY THRESHOLD SHIFT RESULTING FROM NOISE-EXPOSURE

ARAM GLORIG, M.D.

ANNE SUMMERFIELD, PH.D.

(By invitation)

W. DIXON WARD, PH.D.*

(By invitation)

LOS ANGELES, CALIF.

II

The general feasibility of studies of noise-induced temporary auditory threshold shift was established by the pilot experiment reported in the preceding section. In this experiment, the apparatus, the subjects and the temporary shift itself were all found to be sufficiently stable to justify further experiments. For example, there was no systematic change in pre-exposure thresholds from one exposure day to another in any of the 99 normal hearing subjects who participated in the pilot experiment. That is, no permanent hearing loss was produced in any of the subjects. Also, control group data indicated that practice effects did not influence the results of the experiment and it was decided to carry on subsequent research with only one group of subjects. These subsequent studies are now underway.

The apparatus is essentially the same as that used in the pilot experiment except for an additional stepping switch which automatically controls the timing of the experiment procedure. This switch a) controls lights that indicate which subject is to be tested, b) switches the appropriate test frequency to the ear under test, c) grounds the ear phone on the other ear, d) turns the noise on and off.

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* Research Center Subcommittee on Noise

Temporary threshold shifts are measured at 1000 cps and 4000 cps only. A report follows of the results of current studies carried on with a group of 15 normal hearing subjects.

CURRENT EXPERIMENTS

TTS Produced by Intermittent Noise-Exposure. In these experiments, subjects were exposed to bursts of noise in one of three different repeating patterns; namely, on 30 sec-off 30 sec, on 30 sec-off 60 sec, or on 60 sec-off 30 sec. Measurements of the growth of TTS during these intermittent exposures showed:

1) The growth of TTS at 4000 cps is linear when plotted against the logarithm of the exposure time and the rate of growth is approximately proportional to the fraction of the time that the noise is on. If the noise is on half the time the rate of growth of the temporary shift is just half as rapid as the rate for continuous exposure to the noise. If the noise is on two-thirds of the time the log time rate of growth is two-thirds that for continuous noise-exposure, etc. These data are plotted in Figure 1.

2) The rate of growth of TTS increases with the sound pressure level of the exposure noise: specifically, the rate of growth is proportional to the number of db by which the exposure noise exceeds 85 db.

These data, which describe only the temporary threshold shift produced at 4000 cps, are plotted in Figure 2.

The effect of lengthening the bursts of noise to periods of 15 minutes on and 15 minues off is now under investigation. The effect of shorter bursts has been reported by other investigators. The curves plotted in Figure 1 do not apply if the noise bursts are 125 milliseconds or less. More TTS is produced by these shorter bursts than is predicted by our curves. For the time being our results predict only the TTS produced by noise bursts lasting from one quarter second to one minute.

In the experiments reported so far noise bursts were alternated with periods of silence. In most industrial settings, however, it is common for noises of a higher level to alternate with noises of a

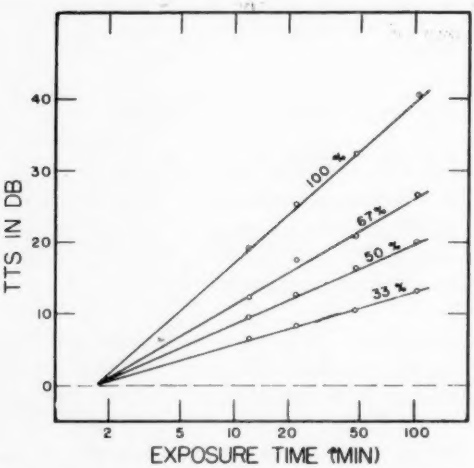


Fig. 1.—Growth of TTS at 4000 cps for various intermittent noise-exposures. Each line represents the TTS produced when the noise is on the indicated percentage of the exposure period. The 50 per cent curve, for example, represents the TTS produced during a two hour period when the noise was on 30 sec—off 30 sec—on 30 sec etc.

lower level, and not with complete silence. What TTS is produced under these circumstances? We assume that in this up-down situation each noise contributes its share to the growth of TTS according to its level and to the fraction of time it is on. The results of a test of this assumption are shown in Figure 3. A noise consisting of alternate 30 second periods of 106 db and of 96 db produced the TTS represented by the points on the graph. The top line in the figure is the TTS produced by 106 db of continuous noise, the lower line by 96 db continuous. The middle line is the TTS to be expected if the assumption is correct. This line is also the TTS expected from exposure to 101 db continuous noise. The excellent agreement between the assumed TTS and the empirical points indicates that the auditory effects of alternating noise levels can be predicted satisfactorily.

Recovery from Temporary Threshold Shift at 4000 cps. If the temporary threshold shift at 4000 cps is less than 50 db the rate of

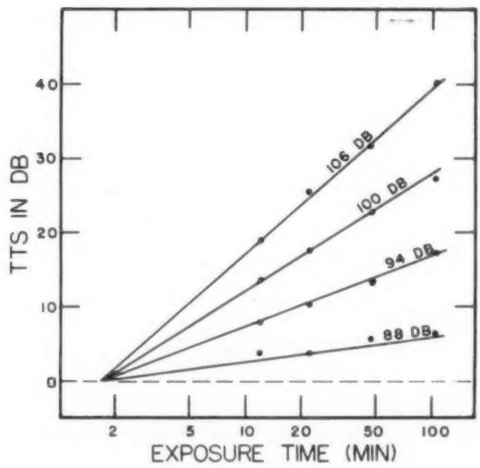


Fig. 2.—Growth of TTS at 4000 cps produced by exposure to continuous noise at the indicated sound pressure levels.

recovery seems to be proportional to the initial magnitude of the shift. Shifts in excess of 50 db recover at a much slower rate than do smaller shifts. Recovery of temporary threshold shift at 4000 cps after two hours of exposure to high level noise is shown as a function of the logarithm of the recovery time in Figure 4. The dashed lines represent two different sub-groups of ears exposed to continuous noise at 106 db. Four ears developed a temporary shift more tha n50 db (upper curve), 22 ears developed temporary shifts less than 50 db.

There is some indication in later data that the rate of recovery may prove to be a function of the time of existence of the TTS as well as of its magnitude.

TTS at 1000 *cps.* The temporary threshold shift produced in normal hearing subjects at 1000 cps by exposure to flat broad band noise is smaller than the shift at 4000 cps. The growth and decay of TTS at 1000 cps as shown in Figure 5 exhibit the same general characteristic behavior as TTS at 4000 cps but the amount of shift

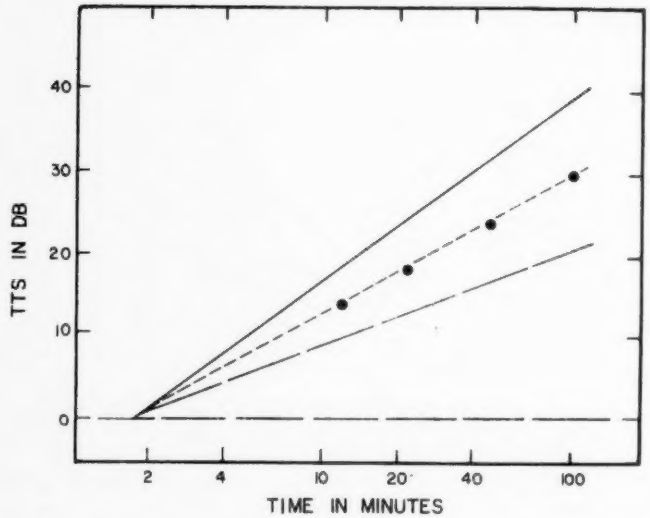


Fig. 3.—Predicted and observed values of TTS at 4000 cps produced during stimulation by a noise that alternated between 106 db and 96 db sound pressure level. The three lines show the expected values for 106, 101 and 96 db respectively from top to bottom. The points are mean values of measured TTS's.

and its rate of production are much smaller for any given exposure. Further, the introduction of short periods of silence reduces the TTS more at 1000 cps than at 4000 cps.

TTS Produced by Octave Bands of Noise. The temporary shift produced by exposure to octave bands of noise is of particular interest to us as a possible means of assessing noise-exposure. First, if some measure of TTS can be taken as an indicator of the severity of noise-exposure and, second, if we can predict this measure of TTS from the known composition of the noise and distribution of the exposure; then perhaps we can set up a general multiple regression equation to predict the severity of any given noise-exposure directly from a combination of properly weighted octave band levels of the noise. We have learned so far that the maximum shift produced

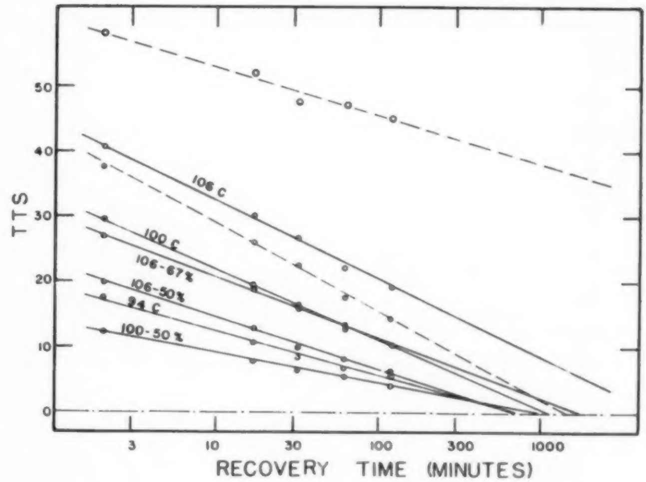


Fig. 4.—Recovery of TTS at 4000 cps after two hours of exposure to broad band noise. The dashed lines represented two different sub-groups of ears exposed to 106 db of continuous noise. The upper curve shows the recovery of four ears that had initial shifts larger than 50 db. The other 22 ears had initial TTS's less than 50 db. The solid lines show recovery for various other exposure conditions. The first number above each line is the exposure noise level in db. The percentage of time the noise was on is given by the second number; C signifies continuous or 100 per cent time on.

by an octave band of noise usually occurs at a frequency that is one-half octave or one octave above the nominal high frequency cut-off of the exposure band. Also, the higher octave bands of noise produce larger TTS's at the frequencies of maximum shift.

COMMENT AND SPECULATION

Explanation of the behavior of the TTS observed in these preliminary studies provides an attractive opportunity for speculation. The senior author of this paper has availed himself of this opportunity and hereby takes full responsibility for the discussion and the speculative statements which follow.

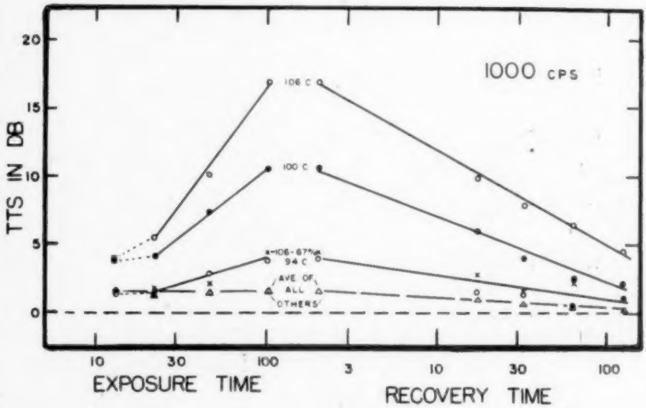


Fig. 5.—Growth and recovery of TTS at 1000 cps; 106 C, for example, indicates continuous exposure to 106 db of noise.

The mechanism of production of TTS is not well understood. The term "temporary threshold shift" is strictly an operational term and in no way describes the physiological process that produces the shift in threshold. That the effect occurs in the organ of Corti or in its neighboring structures is quite well established. Some have suggested that TTS results from a change in the central nuclei but in general this suggestion has not been accepted. A central process cannot account, for example, for the fact that if a man is exposed to high level noise when one ear is fitted with a protector and the other is not, the protected ear shows no shift but TTS does occur in the opposite ear.

Probably the most widely accepted explanation of the shift is based on the concept of fatigue of the peripheral organ. Most evidence points to an electrochemical change which renders the hair cell or its connecting structures incapable of firing or which blocks the normal conduction of the nerve impulse.

Let us speculate on the possibility that excessive auditory stimulation produces an acceleration of the metabolic process. Our TTS

data from intermittent exposure lend support to such an hypothesis. An extension of the curves in Figure 1 show that when subjects were exposed to continuous noise for two hours, the resulting TTS will be almost twice as large as the shift produced by four hours of exposure to an intermittent 30-second-on-30-second-off pattern of the same noise. The total acoustic energy is the same in both exposures, but it appears that if the end organ is allowed to rest between assaults or, in other words, is given a chance to recuperate its losses or to recharge its battery if you will, it responds with a smaller temporary change. Also, the end organ may respond with a smaller permanent change if the long term exposure to a given amount of acoustic energy is intermittent rather than continuous. The evidence to support this latter statement is tentative but we have found, for example, that in some industries riveters whose ears are exposed continuously develop more permanent hearing loss than do jet flight line mechanics.

Another phenomenon to be explained is the time rate of growth of TTS. Our data show that temporary shift growth and recovery changes occur rapidly at first but that there is a decrease in rate of change as time increases. This decrease in rate of change could be explained by a systematic change in cell populations oriented transversely across the basilar membrane from outer hair cell rows to inner hair cell rows. The systematic change would be from cells that respond to stimuli at normal threshold levels to cells that respond only to above-normal threshold stimuli. These latter cells also would require more energy to produce a given measurable change in threshold. The initial rapid growth of TTS would result from the temporary depletion of the more sensitive cells and the later slower growth would be typical of the behavior of the above-threshold cells. It is a moot point whether cell populations actually are ordered across the basilar membrane in a pattern of decreasing sensitivity or whether they respond at increasingly higher sound pressure levels only because of their position transversely and longitudinally on the membrane. We do know that the amplitude of basilar membrane motion decreases in the direction of the modiolus because the membrane is more firmly attached at the modiolar edge.

The concept of a system of cells with different sensitivities is appealing because it could also be used to explain recruitment. Recruitment is not necessarily unique to an impaired cochlea. Equal loudness curves evidence the fact that recruitment occurs in normal

ears. True, recruitment is said to be an abnormal increase in loudness; but this so-called abnormal increase found in the impaired cochlea could be due to just the normal response of normally above-threshold cell populations. When an impaired ear demonstrates recruitment it may be responding as normal ears do at the higher sound pressure levels. The cell populations that ordinarily respond to lower sound pressure levels do not take part in the growth of loudness, however, and this lack could produce what appears to be an abnormal increase in loudness when the elevated threshold is finally passed.

CONCLUSIONS

1. The temporary auditory threshold shift is essentially a stable and consistently repeatable phenomenon both in groups and in individuals.

2. Within certain limitations a) the rate of growth and of recovery of TTS is linearly related to logarithmic increases in time; b) the rate of growth of TTS increases with the sound pressure level of the exposure noise: specifically for our exposures the rate of growth is proportional to the number of db by which the exposure noise exceeds 85 db; c) the amount of TTS produced by intermittent noise-exposure is directly proportional to the on-fraction of the exposure noise, not to the total energy or to the total exposure time.

3. Measurement of TTS appears to be a possible method of assessing noise-exposures.

4. Studies of the temporary threshold shift should provide valuable information about permanent threshold shift. Specifically, measurements of the TTS produced by exposure to a given noise may eventually be used to predict the amount of permanent threshold shift to be expected from extended exposure to that noise.

RESUMÉ

The results of a series of studies of the temporary auditory threshold shift produced in normal ears by exposure to broad band noise show that

1) The temporary threshold shift produced by intermittent exposure to noise is significantly less than the shift produced by continuous exposure to the same total amount of noise.

2) The temporary threshold shift produced at 4000 cps by exposure to broad band noise is significantly larger than the shift at 1000 cps.

3) At 4000 cps temporary threshold shifts of more than 50 db recover much more slowly than do shifts of less than 50 db.

4) The maximum shift produced by exposure to octave bands of noise occurs, on the average, one-half octave to one octave above the nominal high cut off frequency of the exposure band.

111 North Bonnie Brae St.

LXII

DIFFERENTIAL DIAGNOSIS BETWEEN OTOSCLEROSIS AND CONGENITAL FOOTPLATE FIXATION

HOWARD P. HOUSE, M.D.

LOS ANGELES, CALIF.

Shambaugh,[1] in an article published in 1952 describing developmental anomalies of sound-conducting apparatus, described five cases that he had operated upon with a patent meatus, an intact tympanic membrane, but with congenital stapes fixation. Holmgren,[2] in an article published in September 1957, briefly described the surgical findings of a case of bilateral incomplete development of the oval window. I am sure others have observed congenital abnormalities in this region, but our review of the literature has failed to reveal any other specific writings on this subject.

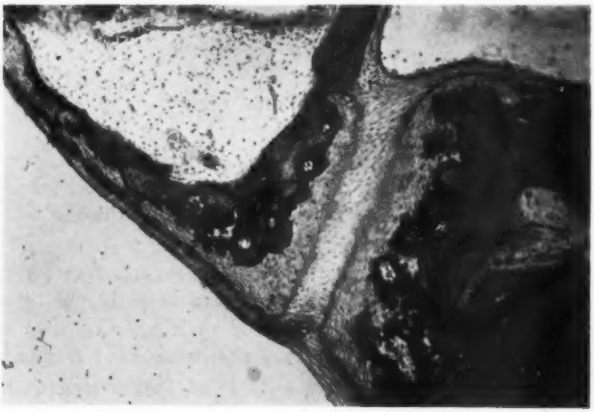
The malleus and the incus are differentiated from the first branchial arch, or Meckel's cartilage, and failure to differentiate results in a deformed or fused malleus and incus. The ear drum, the external ear canal, and the auricle may also be involved.

The stapes is derived from the second branchial arch, or Reichert's cartilage. It seems logical that failure to differentiate would result in an abnormality of the stapes. Altmann[3] described the histologic findings of a case of atresia with stapes fixation. Wolff[4] has also described abnormalities in the annular ligament of the newborn.

In an effort to better understand clinical otosclerosis in children, we recently reviewed our cases under 12 years of age, who had a conductive loss with essentially normal otologic findings, and who

From the Department of Otolaryngology, University of Southern California School of Medicine.

Sponsored by the Los Angeles Foundation of Otology.



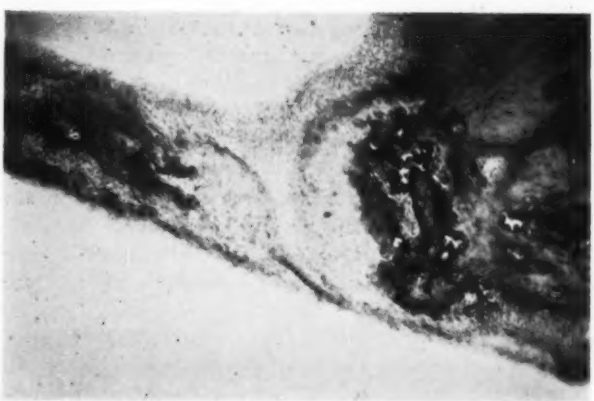


Fig. 1 Fig. 2

Abnormalities in the ligament of the newborn.

(From the Laboratory of the Manhattan Eye, Ear and Throat Hospital; Courtesy of Dorothy Wolff, Ph.D., and Richard Bellucci, M.D.)

LONG TERM STUDY OF CONDUCTIVE LOSSES IN CHILDREN

were examined in our office ten or more years ago. We located as many as possible and had them return for re-evaluation of their hearing. These cases can be classified into four groups.

Group 1. Group 1 were children with conductive losses of 15 to 35 decibels in the three speech frequencies, who responded to therapy and who had no further difficulty in adulthood.

Group 2. Group 2 were children with conductive losses of 15 to 35 decibels, who did not respond satisfactorily to therapy in childhood. This group usually regained their hearing after adolescence, apparently due to spontaneous regression of lymphoid tissue. Rarely, one may find in this group cases of very minor deformities in the ossicular chain. In this instance, the conductive loss would remain unchanged in adulthood.

Group 3. Group 3 were children with conductive losses of 15 to 35 decibels, who progressed to further loss in adulthood. This further progression was apparently due to otosclerosis. Subsequent surgery on this group is proving this diagnosis to be correct.

Group 4. Group 4 were children with a marked conductive loss in childhood, averaging 45 to 55 decibels in the three speech frequencies. This group showed the same degree of loss in adulthood ten or more years later. This lack of progression would suggest congenital ossicular fixation and subsequent surgery being performed on this group reveals the fixation to be present usually at the stapes footplate region.

DIFFERENTIAL DIAGNOSIS BETWEEN CLINICAL OTOSCLEROSIS AND CONGENITAL FOOTPLATE FIXATION IN THE CHILD

In a child under 12 years of age the diagnosis of clinical otosclerosis is difficult because the key factor of progression cannot be definitely established. If a child has a conductive loss not to exceed 35 decibels in the three speech frequencies, has essentially normal physical findings, and does not respond to routine otologic therapy,

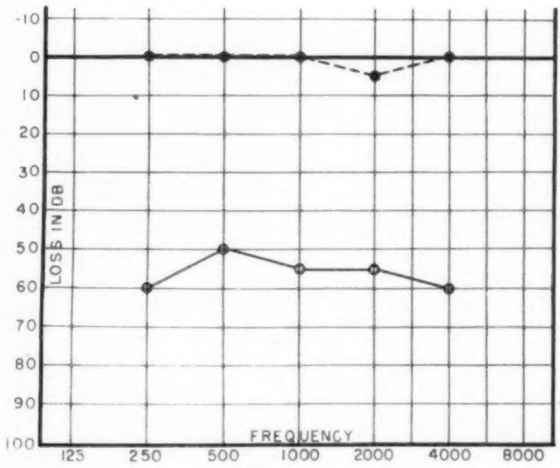


Fig. 3.—Characteristic audiogram of congenital footplate fixation.

the diagnosis may be clinical otosclerosis. Confirmation of this tentative diagnosis can only be achieved by noting a progression of the hearing loss, which often is rapid during the period of adolescence, or by surgical exploration and examination of the stapes footplate.

The diagnosis of congenital footplate fixation in children is based on normal physical findings and the characteristic flat 45 to 55 decibel pure conductive loss with a normal bone conduction curve.

Children with congenital footplate fixation are often slow to develop speech and are all excellent lipreaders. The accurate determination of lack of progression in these cases is often difficult. Usually there is a history of accidental discovery of the hearing impairment, either by school tests or as the result of a certain incident which called attention to their hearing deficiency. After discovery the child and the parents become suddenly aware of the impairment and proceed to test the hearing acuity in various ways. By concentrating on the problem the individual involved, as well as the relatives, often may feel the hearing is getting worse when actually they are only

becoming more aware of the pre-existing deficiency. As the child grows older it may also seem the loss is becoming greater because of the increased demands made on his hearing by his more adult activities.

In view of our long term studies of conductive impairment in children, it seems logical that any child under twelve years of age with normal physical findings, who has a purely conductive hearing impairment approximating 50 decibels, has congenital footplate fixation rather than clinical otosclerosis. An analysis of our operated cases of congenital footplate fixation in children confirms this hypothesis. Eighty-five per cent of our series noted the hearing loss before they were 12 years of age.

DIFFERENTIAL DIAGNOSIS BETWEEN CLINICAL OTOSCLEROSIS AND CONGENITAL FOOTPLATE FIXATION IN THE ADULT

The differential diagnosis between clinical otosclerosis and congenital footplate fixation in the adult depends primarily on a definite history of progression of the hearing impairment.

An adult with a history of a slowly progressive hearing loss, who has a conductive or mixed type impairment and essentially normal otologic findings, may be diagnosed as clinical otosclerosis.

An adult with a history of a non-progressive hearing impairment, who has a pure conductive loss of 45 to 55 decibels and has essentially normal otologic findings, may be diagnosed as a congenital ossicular deformity, which is most commonly fixation occurring at the stapes footplate.

OBSERVATIONS AT SURGERY

Surgical exploration by the stapes mobilization approach reveals rather characteristic findings in cases of congenital footplate fixation.

The normal stapes footplate has a characteristic appearance. There is no increase in vascularity of the mucous membrane about

Fig. 4.—Normal stapes footplate.

the footplate region. The margins of the footplate and the annular ligament are distinct. The central portion of the footplate is often thin and usually has a bluish appearance. Gentle palpation reveals uniform mobility.

In otosclerosis there often is an increased vascularity of the mucous membrane surrounding the footplate, usually in the anterior area. The margins of the footplate and the annular ligament are often difficult to visualize, especially anteriorly because the otosclerotic bone frequently engulfs this area. The central portion of the footplate is often thin with a bluish discoloration. Whitish otosclerotic plaques are often seen spreading over the surrounding bone of the otic capsule. Palpation reveals fixation of the footplate, usually in the anterior region.

In congenital footplate fixation there is no increase in vascularity of the mucous membrane surrounding the footplate area. The central portion of the footplate is not thin and the bluish discoloration is usually not present. The margins of the footplate and the annular ligament are difficult to visualize since the entire footplate bone blends

Fig. 5.—Otosclerotic footplate fixation.

Fig. 6.—Congenital footplate fixation.

into the bone of the surrounding otic capsule. This diffuse bony fusion may be thick or thin. If thin, the footplate can often be readily mobilized; if thick, mobilization may be very difficult. Gentle palpation reveals uniform and total fixation of the entire footplate.

AN ANALYSIS OF TWENTY-SIX OPERATED CASES

Twenty-six cases of suspected congenital footplate fixation were explored by the stapes mobilization approach. This represents approximately 1% of our mobilized series. The youngest was six years and the oldest was sixty years of age. All of these cases happened to be bilateral, but I am sure there is also a relatively high incidence of unilateral congenital stapes fixation.

Fifty per cent of this series attained a 30 decibel level three weeks following mobilization. Those that were not successfully mobilized, who were subsequently fenestrated, obtained serviceable hearing.

PERMANENCY

This series of cases of congenital footplate fixation is too small and the time factor too short to establish conclusions in regard to permanency. Some improve and regress and others mobilized successfully over one year ago seem to be maintaining their postsurgical hearing improvement.

SUMMARY

	Otosclerosis	*Congenital*
HISTORY		
Progression	Present	Not present
Age of discovery	Young adulthood	Childhood
Speech development	Average	Slow
Family history	Often positive	Seldom positive
Tinnitus	Often present	Seldom present

PHYSICAL EXAMINATION		
	Essentially normal (May show pink promontory)	Essentially normal (Does not show pink promontory)
AUDIOMETRIC FINDINGS		
Air conduction curve	Greater loss in low frequencies	Flat over entire frequency range
Amount of loss	Varies with degree of fixation	Approximately 50 dbs indicating total fixation
	Otosclerosis	*Congenital*
Cochlear involvement	Common	Rare
Bone conduction curve	Frequently drops in higher frequencies	Usually does not drop in higher frequencies
SURGICAL OBSERVATIONS		
Vascularity of middle ear mucosa	Often increased especially anteriorly	No increase in vascularity
Central footplate area	Usually thin and bluish	Seldom thin or bluish
Appearance of bone surrounding oval window	Whitish plaques often present	No whitish plaques present
Appearance of footplate margins and annular ligament	Readily distinguishable especially posteriorly	Not readily distinguishable
Degree of fixation	Partial to total	Total
Primary location of fixation	Usually anterior	Uniform throughout
Mobilization	Average case less difficult	Average case more difficult
Fenestration	Some are not suitable	All are suitable

CONCLUSIONS

1. Congenital footplate fixation is a definite entity which can be diagnosed clinically and confirmed at surgery.

2. In the child the diagnosis of congenital footplate fixation is based on the classical audiometric findings. In the adult the diagnosis is based on a lack of progression, as well as the typical audiometric findings.

3. Patients with congenital footplate fixation are very suitable candidates for surgery since the cohlear function is essentially normal.

4. Mobilization in cases of congenital footplate fixation is usually more difficult than in cases of otosclerotic fixation. If the footplate cannot be successfully mobilized, the patient is an ideal candidate for subsequent fenestration surgery.

1136 West Sixth St.

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LXIII

PRESSURES OF THE LABYRINTHINE FLUIDS

FRANCIS L. WEILLE, M.D.

AND

JOHN W. IRWIN, M.D.

GEZA JAKO, M.D.

LINA L. HOLSCHUH, A.B.

A. SANDYLEE WEILLE, A.B.

CAROL A. STANLEY, A.B.

MAURICE B. RAPPAPORT, E.E.

(By invitation)

BOSTON, MASS.

Hearing, one of the complex sensory phenomena, has been studied by many investigators for centuries. Various intricate techniques have been employed, especially during the present generation. Many facets are not thoroughly understood. It is now obvious that a complete understanding of this highly organized biological system will not come through the pursuit of any one approach, be it philosophical, anatomical, physiological, biochemical, or physical, but rather by the combined efforts of individuals trained in various fields of endeavor. In this manner, ideas and experiments may be exchanged. This paper reflects the teamwork of one segment of such a group.

The circulation of the labyrinthine fluids is undoubtedly a dynamic biological process. In determination of the source and disposition of perilymph and endolymph, it is important to know the pressures of these fluids in living animals. Szasz[1,2] attempted to measure the pressure of perilymph in living dogs. He used capillary

From the Department of Otolaryngology at the Massachusetts Eye and Ear Infirmary and Harvard University. This investigation was supported in part by research grant B-1344, National Institute of Neurological Diseases and Blindness of the National Institutes of Health, Public Health Service, and in part by the Eaton-Peabody Fund.

tubes 25 to 30 cm long with internal diameters of 0.5 to 0.75 mm. The capillary tube was partially filled with colored physiological saline (1 to 2 mm), and then the tube was inserted through the membrane of the round window. He measured the distance the colored liquid moved up the tube and found this to be 20 to 60 mm. Due to capillary resistance such measurements would represent relative, but not absolute, pressure. He observed that an elevation in spinal fluid pressure increased the perilymphatic pressure. When he tried to measure pressure in dead dogs, he always obtained a zero reading.

At the Massachusetts Eye and Ear Infirmary during the past three years, pressures of both perilymph and endolymph have been measured in living guinea pigs in terms of millimeters of mercury. The development of the electromanometer has made this possible.

METHODS

The experimental animal was the guinea pig. Sodium pentobarbital was used for anesthesia; the initial intraperitoneal dose was 40-45 mg per kilogram. Additional doses sufficient to maintain deep anesthesia were given as required throughout the experiment. Most guinea pigs received a constant supply of moistened oxygen via an intratracheal cannula during the experiments in order to suppress respiratory movements. Such a method has been described previously by Irwin and Macdonald.[3]

An incision was made from the midventral line of the neck to the mandible just above the area where the anterior and posterior facial veins approach the masseter muscle. Careful dissection separated the sheath of the external jugular vein from the masseter muscle. The tissue and blood vessels were pushed to the medial side of the masseter muscle; then the mandible was fractured. A retractor was used to clear the area between the mandible and soft tissues of the neck. The exposed sternocleidomastoid muscle was severed. The posterior belly of the digastric muscle was removed, and with blunt dissection the bulla cell was brought into view; this was opened with a small rongeur to expose the cochlea.

With the aid of a binocular dissecting microscope (10X-40X), the second or third turn of the cochlea was located. A band of pig-

mented cells marked the area of the stria vascularis. Within the limits of this band a fenestra about 30-40 micra in diameter was made when the pressure of the endolymph was to be measured. If determination of the pressure of perilymph were desired, a fenestra of similar size just above or below the pigmented band was constructed. Fenestrae were fashioned with a hand drill having a cutting burr 20 micra in diameter; some were made under fluid, and others were made under dry conditions. Several larger fenestrae, averaging about 250 micra, were made by methods described by Weille et al.[4]

Pressure measurements of perilymph through the round window were made using the following surgical approach: the guinea pig on the animal holder was placed under a Zeiss binocular dissecting microscope, and the orifice of the external auditory canal and tympanic membrane were visualized. Two parallel incisions were made in the upper and lower part of the external canal and were continued outside into the cartilage of the auricle. These two incisions were joined by another which was half-curved at the edge of the orifice of the external canal. The soft tissues and periosteum were separated from the posterior bony part of the external canal, and the wound edges were held back by an iris retractor. At this point, all the cartilage of the external canal was removed. Then the posterior bony external canal was dissected with a fine rongeur, care being taken not to injure the tegmen or the dura. The facial nerve was bisected, but not stripped. The semicircular canals were not molested. With the removal of the posterior bony part of the external canal, the posterior edge of the tympanic membrane was detached and pushed forward by a needle as in stapes mobilization. Care must be taken not to push hard or dislocate the ossicles. With this approach the round window and its membrane and the ossicles, including the footplate of stapes, were well visualized. The motion of the round window membrane was noted by moving the ossicles. Vessels in the round window membrane and the first turn of lamina spiralis ossea were usually observed. The form, position, and location of the round window in the bony cochlea generally were the same, but small deviations occurred. The membrane itself was quite vulnerable. This endaural transmeatal approach gave adequate exposure for cannulization of the perilymphatic space.

In these experiments, a capacitance electromanometer was used. This capacitance manometer consisted of a fixed metal plate which

was parallel to, and 0.001 inch from, a stiff flexible, metal membrane. One side of the flexible membrane was exposed to atmospheric pressure; the other side was acted upon by the pressure to be measured. If the pressure applied were higher than atmospheric, the flexible membrane would bend toward the fixed plate, thus increasing the electrical capacitance of the transducer. If the pressure were negative, the flexible membrane would bulge away from the fixed plate to reduce the electrical capacitance.

The radio frequency oscillator developed a constant voltage of about 230 kilocycles per second. The oscillator voltage was applied to a bridge circut, one arm of which contained the manometric transducer. The bridge was electrically balanced with both sides of the transducer membrane at atmospheric pressure by means of a variable condenser. Two fixed condensers were always kept equal. Equal voltages appeared at the two output terminals of the bridge. When pressure was applied to the transducer, the capacitance was changed and the bridge was unbalanced. A voltage difference proportional to the degree of unbalance appeared at the output of the bridge. This voltage difference was amplified by the radio frequency amplifier. Thus a radio frequency voltage existed, the amplitude of which fluctuated as pressure changed. A detector and its associated filter circuit removed the radio frequency components of this voltage, leaving only the voltage fluctuations proportional to pressure.

In these experiments, a standard Sanborn Electromanometer and a Sanborn Model 62 dual channel recorder were used. A mobile coaxial cable (CPH Amphenol RC 69/U) connected the microphone to the bridge. A plastic adapter connecting the microcannula to the microphone was screwed on tightly with the aid of stop-cock lubricant to exclude air.

The microcannulas were made from quartz or pyrex tubing 1-3 mm O.D. with T 5/20 female joint. The pyrex microcannulas were made in the laboratory. The pyrex tubing was pulled in a hot flame of a blast burner to a fine point; the cannula then was inserted into a de Fonbrune microforge. The tip was heated and drawn to a short point of no more than 75 micra, with the internal diameter of its orifice being 25 to 35 micra. The total length of the cannula was not allowed to exceed 7.5 cm.

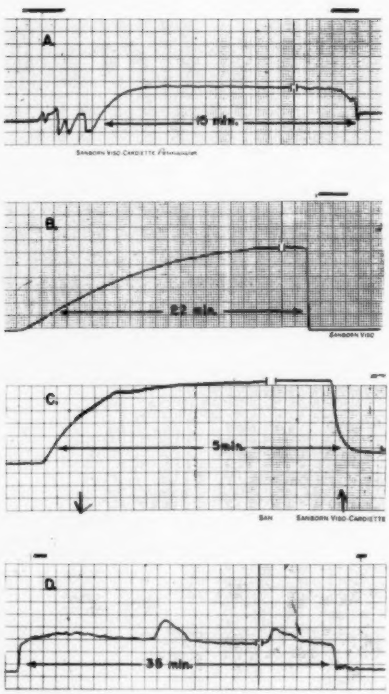

Fig. 1.—Each tiny square equals 0.04 second. Each large square equals 0.20 second. A. Pressure curve of endolymph through a fenestra of about 250 micra. B. Pressure curve of endolymph through a microfenestra of about 30 micra. C. Pressure curve of perilymph through a microfenestra of about 30 micra. D. Pressure curve of perilymph through membrane of round window.

The microphone, adapter, and cannula were filled with Ringer's solution. It was important that no air bubbles be permitted within the system and that the microcannula be filled to its very tip.

The microphone, adapter, and microcannula were fitted to the micromanipulator; with the latter and a microscope, the tip of the cannula was inserted into perilymph through the round window or

appropriate fenestra or into the endolymph through the correct fenestra.

When the pressuregram was obtained, it was calibrated in terms of mm of mercury with a correction for the column of fluid in the microcannula and reservoir. The living anesthetized guinea pig was then decapitated in 29 experiments. The skull was fixed in 10 per cent formalin solution for 24 hours. In two animals perfusion through the aorta with filtered Heidenhain-Susa solution was the method of fixation. Several days were allowed for decalcification in trichloracetic acid. Then the preparation was dehydrated by running through alcohols and finally embedded in celloidin. Serial sections 16 micra thick were made using a sledge microtome (Leitz "Wetzlar") and mounted after staining with Harris hematoxylin and water-soluble eosin. These sections were prepared from a number of animals to demonstrate the correct insertion of the cannula.

RESULTS

When a large area of the spiral ligament was exposed at one turn of the cochlea, the pigmented cells and attachments of Reissner's membrane and the basilar membrane could be visualized well with a microscope. One hundred and thirty-five such fenestrae were made, and measurement of the pressure of endolymph was attempted in all. In 101, however, the spiral ligament was detached by the entry of the tip of the cannula, and no pressuregrams were obtained. Pressure curves were secured in 34. Figure 1A is one such pressuregram. The height of this curve was maintained for 15 minutes before the tip of the microcannula was withdrawn. This particular pressuregram calibrated to 8 mm Hg. Figure 2A graphically presents the various pressures recorded in the 34 successful experiments. These pressures averaged 7.5 mm Hg with the spread being from 2-13 Hg. Since most pressures fell in the range of 10 mm Hg, it seems probable that the lower pressures in the area of 2-6 mm Hg were secured in animals in which the microcannula had torn the spiral ligament allowing some endolymph to escape. No histological preparations were made of the cochleae of these experimental animals.

Because there was considerable doubt as to the loss of endolymph with the large fenestrae, a change was made to the microfenestrae.

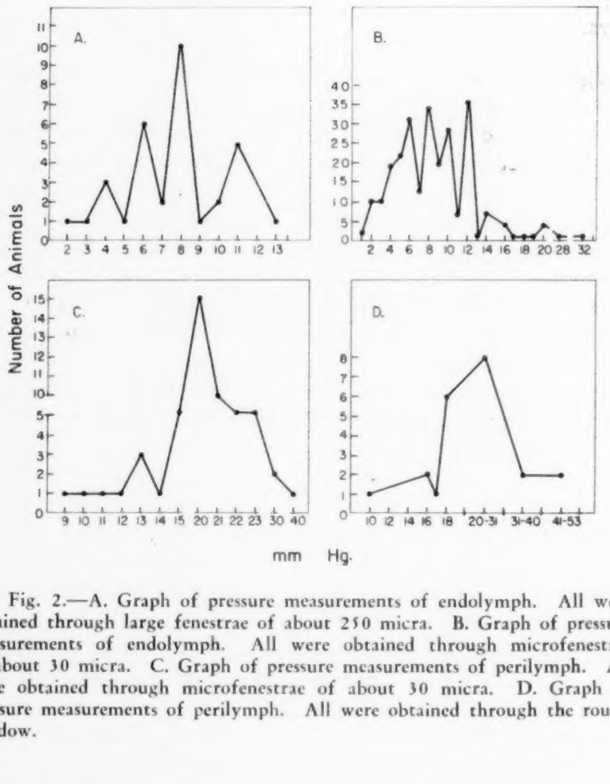

Fig. 2.—A. Graph of pressure measurements of endolymph. All were obtained through large fenestrae of about 250 micra. B. Graph of pressure measurements of endolymph. All were obtained through microfenestrae of about 30 micra. C. Graph of pressure measurements of perilymph. All were obtained through microfenestrae of about 30 micra. D. Graph of pressure measurements of perilymph. All were obtained through the round window.

In all, 431 small fenestrae have been made in the area of the pigmented cells, and in 252, pressures were recorded. Figure 1B is one pressuregram of this series. The height of this curve was maintained for 24 minutes before the tip of the microcannula was removed from the endolymph. This pressure calibrated to 8 mm Hg. Figure 3 is a microphotograph of a section of this cochlea, and it shows that the tip of the microcannula was in endolymph. In 30 other experiments, similar histological preparations were made, but in only 2 of the 31 was it clear that the end of the microcannula was in endolymph. Histological error led to discard of the preparations in 5. Six showed that the microcannulae had entered perilymph, and it is of

interest that these pressures varied from 14 mm to 32 mm Hg. Eighteen showed that the spiral ligament was torn away or had not been pierced. These could be interpreted as failures to place the tips of the cannulae in endolymph or as artefacts in histological technique. Obviously, many more such histological preparations must be made from cochleae in which endolymphatic pressure has been measured. Figure 2B shows the various pressures recorded in the 252 experiments. These pressures averaged 8.5 mm Hg, with the lowest recorded as 1 mm Hg and the largest as 32 mm Hg. It is difficult to explain the larger pressures. Perhaps in these instances the tips of the microcannulae entered perilymph, as some histological sections suggested. The lower pressures could have been due to the loss of endolymph before the pressurgram was recorded.

In 110 guinea pigs, microfenestrae were made just above or below the area of the pigmented cells either in the second or third turns. Pressuregrams were recorded in 51 of these guinea pigs. Figure 1C is one of these pressuregrams. The height of the curve was maintained for five minutes before the microcannula was withdrawn from perilymph. This curve calibrated to 22 mm Hg. Figure 2C graphs the various pressures recorded in these 51 experiments. These pressures averaged 24 mm Hg with a spread from 9 to 40 mm Hg. To date, none of the cochleae prepared from these experiments are ready for sectioning. The lower pressures might either represent partial loss of perilymph or entry of the microcannulae into endolymph.

Attempts in 100 guinea pigs were made to secure a pressure of perilymph through the round window. Pressuregrams were satisfactory in only 21. There was the problem of tearing the membrane of the round window with the tip of the cannula. Figure 1D is one of these pressuregrams. It calibrated to 28 mm Hg, and the height of the curve was held for 35 minutes before the end of the cannula was withdrawn from the perilymph. The humps in the curve occurred when the guinea pig breathed, suggesting an increase in perilymphatic pressure during inspiration. Figure 2D charts the 21 pressures secured. The lowest was 10 mm Hg, and the highest 52 mm Hg; the average of all pressures was 25 mm Hg. No histological studies were done in this series of experiments.

In these experiments a number of guinea pigs expired during surgery. In each instance the experiment was completed, and at-

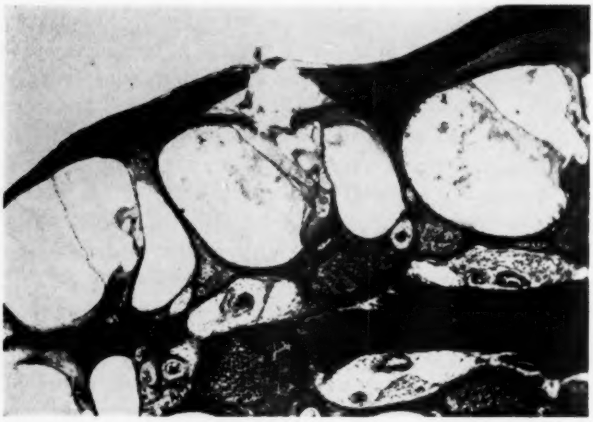

Fig. 3

tempts to secure pressures of both endolymph and perilymph were attempted. No pressuregram was ever secured in these dead animals.

COMMENT

Experimental results here cited indicate that the pressure of perilymph is higher than that of endolymph. If such is the case, Reissner's membrane, which is only two cells thick, would have to be under constant tension. From the strict biological viewpoint, this would be most unlikely. The capacitance manometer described, however, is an accurate instrument, and the variance of the pressures of endolymph and perilymph was consistent even though the means of approach to these fluids varied. It would seem rather unlikely, therefore, that one artefact in technique could account for the persistent pressure variance; the combination of several artefacts always acting in the same direction appears even more improbable. The difference between these experimental data and theory cannot be reconciled at this stage, and obviously another set of experiments is urgently needed. In one animal, simultaneous pressures of endolymph and perilymph must be secured, and, at the same time, it must be deter-

mined whether or not a current will flow between an electrode in the cannula in the scala media and an electrode in the cannula whose tip is in the scala tympani or vestibuli. In the end, histological sections of the cochlea of this same animal must clearly show that the tip of one microcannula was in the scala media and the other was in either the scala tympani or scala vestibuli. Such experiments are now being planned; if they should support the theory based on present data that the pressure of endolymph is lower than that of perilymph, then a study of the biological characteristics of Reissner's membrane will be imperative.

A number of investigators[5-11] have studied the biochemistry of endolymph and perilymph. Smith, Lowry, and Wu[9] and Citron et al[10,11] showed that endolymph was higher in potassium and lower in sodium than perilymph. Both groups found the protein content of perilymph higher than that of endolymph. Naftalin and Harrison[12] considered these factors and plotted an hypothesis for the circulation of the labyrinthine fluids. They favored flow from perilymph through Reissner's membrane to endolymph with the stria vascularis acting as a selective absorbing site. It is of interest that our actual pressuregrams of endolymph and perilymph would favor their hypothesis and that the inability to secure pressuregrams in either the scala media or perilymphatic spaces of dead animals favor the hypothesis of dynamic flow of labyrinthine fluids. To establish such an hypothesis, the exact osmotic pressure relations of perilymph and endolymph must be worked out. It would also appear wise to check further the microchemistry of these two fluids.

All these experiments show clearly that it is possible to use accurate techniques to investigate the inner ear. These techniques open further vistas of investigation for those interested in auditory research.

CONCLUSIONS

1. A method of recording accurate pressuregrams of endolymph and perilymph in living guinea pigs has been described.

2. Initial studies indicate that the pressure of perilymph is greater than that of endolymph.

3. The need for additional experimental work is stressed.

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LXIV

THE DIFFERENTIAL DIAGNOSIS OF VERTIGO

HENRY L. WILLIAMS, M.D.

AND

KENDALL B. CORBIN, M.D.
(By invitation)

ROCHESTER, MINN.

In the differential diagnosis of vertigo, differentiation from Ménière's disease is most important. To make such a differentiation the criteria for the diagnosis of Ménière's disease must be firmly established. Some observers have evinced a skeptical attitude and suggest that Ménière's disease is not a definite nosologic entity, but that it is a disturbance of the labyrinthine system and the central nervous system of diverse causes.

MÉNIÈRE'S DISEASE AND ITS DIFFERENTIAL DIAGNOSIS

In the following paragraphs on Ménière's disease we have had two purposes in mind: 1) to present sufficient background material to allay the skepticism about Ménière's disease's being a disease entity and 2) to present clearly the criteria needed for its diagnosis. To do this, it seems best to use a chronologic approach, developing the description of the disease and the criteria for differential diagnosis from the early clinical observations and hypotheses, finally discussing the pathologic findings and then the physiologic aspects.

In his original description of the disorder Ménière pointed out the episodic character of the vertiginous crises and the tinnitus that might precede the initial attack of vertigo by as long as several years but might appear only with the first crisis. This tinnitus may be intermittent or continuous, is usually of a roaring character and is not altered by carotid pressure; the last testifies to a "nervous origin." Ménière also described the bass deafness in the affected ear which

might precede the onset of the vertiginous crises by many years or might appear only with the initial attack. Thus in the original description differentiation was based largely on the history, the only diagnostic test being that of the hearing. The lack of significant tests undoubtedly was the origin of the diagnostic confusion that arose.

Mygind and Dederding and Crowe pointed out the variability of the hearing loss in the early stages of the symptom complex, and Lillie, Horton, and Thornell showed that in many instances the loss of hearing may be reversed under treatment.

Ménière mentioned four kinds of sensation experienced during the crisis or attack. 1) The patient might experience the sensation that the external world was spinning around him (objective vertigo) or that he himself was spinning in space (subjective vertigo). 2) The patient might experience an up-and-down to-and-fro sensation as "being on the bridge of a ship at the mercy of a stormy sea." 3) The patient might feel and be unsteady; in particular he might have a feeling of lateral pulsion and on attempting to walk might veer to one side and bump into a door jamb, a tree or a wall. 4) The patient without previous warning might fall to the ground as though struck on the head and afterward while lying down experience violent vertigo, nausea, and vomiting. These attacks might persist one to 24 hours. Ménière also noted that a syncopal state with pallor, cold clammy sweat, and a feeble pulse was associated with the crisis. He stated in addition that between the crises of the disorder the patient often was unable to make sudden motions of the head, to roll over in bed or to get up from or recline in a chair or bed without experiencing either vertigo or momentary unsteadiness, although rarely to a severe degree.

He also called attention to the facts of great differential importance that during the attack the patient does not lose consciousness, has no weakness or paralysis, can use the tongue freely and at the termination of the attack can describe the events of the illness without difficulty or confusion.

The Place of the History in the Differential Diagnosis. This description of the symptoms of Ménière's disease should make it obvious that a careful and detailed history is important in the differ-

ential diagnosis of Ménière's disease. This history should preferably be taken chronologically; that is, the date of onset should be noted together with the circumstances surrounding it, especially any unusual tension to which the patient was subjected immediately prior to the onset of symptoms. It should be noted also whether the first symptom was tinnitus, loss of hearing or vertigo. One should be particularly careful to get a description of the sensation the patient experienced in the attack. The words vertigo and dizziness are often used by physicians and laity alike without appreciation of their true meaning. Vertigo in the strict sense is a sensation that the outer world is moving about the person (objective vertigo—eyes open) or that the person himself is whirling in space (subjective vertigo). Dizziness, on the other hand, is a sensation of movement within the head. Vertigo and dizziness may coexist. Sensations of inco-ordination, confusion, drunkenness, or swimming or floating are often described by the patient with the term vertigo or dizziness. It is important for the physician to get as accurate a description as possible from the patient as to the sensation he was experiencing in order to distinguish conditions which may produce these other sensations from Ménière's disease.

Appreciation of the position of the head and body in space is produced by the integration of sensations derived from the proprioceptors, the eyes, and the labyrinthine system. By the labyrinthine system is meant the end-organ, the vestibular nerve, the vestibular nuclei, the medial longitudinal fasciculi, their connections with the nuclei of the ocular muscles and other nuclei in the brain stem and higher centers. Walzl and Mountcastle mapped out the projection of the vestibular nerve to the cerebral cortex of the cat. Foerster found that stimulation of the superior lip of the interparietal sulcus evoked violent vertigo. The patient saw the objects before him moving toward the side of the stimulation but felt that his body was turning toward the opposite side. Penfield, by electrical stimulation to the cortex adjacent to the transverse gyrus of Herschl, produced a sense of turning. All the points of stimulation fell on the first temporal convolution of one side or the other.

Imbalance of any one of these three systems with the other two probably produces confusion in the integrating centers which may result in the sensation of vertigo. According to Alpers the most violent vertigo is produced by abnormal stimulation of the labyrinth-

ine system. Some doubt that symptoms of dizziness and the like are produced by abnormal signals from any of the three systems responsible for equilibrium.

Pathologic Evidence of Ménière's Disease. Ménière expressed the belief that microscopic researches on the labyrinth would reinforce his opinion that the disease had its origin there and would throw some light on the nature of the condition he described. In 1938 Hallpike and Cairns reported the pathologic findings in two cases of authenticated Ménière's disease, and in 1940 Hallpike and Wright gave the pathologic details in another. The pathologic changes in all three cases were similar and were described as consisting primarily of gross dilatation of the ductus cochlearis and secondarily of the saccule and utricle. Degenerative changes were found in the organ of Corti in all three cases and in the stria vascularis of two. Since that time these findings have been confirmed by numerous observers and the pathologic basis of Ménière's disease is considered to be established.

The Physiologic Disturbance. The physiologic disturbance leading to the pathologic changes is considered to be an autonomic disintegration or dysfunction according to the original hypothesis of Petersen. This same functional disorder was later considered by Duke under the term "physical allergy." This hypothesis suggests an inherited constitutional tendency for abnormal reactions in the autonomic system. In a broad sense this system has three components: 1) the tissues in which the physiochemical changes are produced in the cellular and intercellular fluids and at the interfaces, 2) the vascular system which supplies nutrition and 3) the autonomic nervous system which mediates and tends to speed up and localize the reactions. Petersen pointed out that this system is an integrated system and that a reaction in any of the components is immediately reflected by a reaction in the other two. Autonomic dysfunction, therefore, might well be termed "Petersen's syndrome."

The physiologic disturbances of autonomic dysfunction are widespread and changes in the capillary loops in the nail beds were observed by Parrisius and by Müller in patients with Ménière's disease. Autonomic dysfunction of the same type is present in the whole group of disorders termed by Brown the "vasomotor neuroses" including Raynaud's disease, chronic simple glaucoma, acrocyanosis and

migraine. Some observers have suggested that the same type of reaction is present in gastric and duodenal ulcer.

Although abnormal autonomic reactions may be widespread, they tend to produce dysfunction in certain regions or organs. If such a reaction has its major expression in the labyrinth, the symptoms and pathologic findings of Ménière's disease will be produced, although the reactions in the capillaries with the concomitant changes of intravascular agglutination (blood sludging) also may be observed elsewhere in the body.[10]

Indirect evidence that these reactions occur in the labyrinth is good, but since these reactions must be observed during life and the statokinetic and acoustic labyrinths are so well protected from observation, direct evidence of experimentally produced autonomic dysfunction in the labyrinth has been furnished only by Weille and his co-workers.

These changes affect the secreting mechanism of the stria vascularis and result in changes in the endolymph which seem to produce an endolymph of greater osmotic pressure, retention of extracellular fluid, and electrolyte changes which produce the compression of the organ of Corti and the slow variations in hearing[28,46] which are characteristic of the disorder.

On the other hand the sudden crises or attacks of vertigo which are not necessarily synchronous with the acoustic changes are most likely to be caused by sudden vascular changes affecting the cristae ampullares, vestibular nuclei or the higher centers and may produce these same symptoms without affecting the labyrinth. For this reason Ménière pointed out that the cardinal sign of his disorder was the involvement of hearing. Since pathologic studies have confirmed Ménière's hypothesis, it is necessary to differentiate episodic vertigo without labyrinthine involvement from Ménière's disease itself. The reason for this is that in Ménière's disease, although vasospasm on the basis of autonomic dysfunction may or may not affect the blood supply of the central nuclei, it affects the blood supply of the labyrinth, particularly the labyrinthine artery, and the capillaries of the stria vascularis. This results in fluid and electrolyte changes in the endolymph which are not present when vasospasm affects the higher centers alone. Therapeutic relief of true Ménière's disease,

therefore, is much more difficult than relief of episodic vertigo from vascular changes in the central nervous system. To achieve success in the treatment of Ménière's disease, other forms of episodic vertigo must be carefully distinguished.

Tests of Functional Derangements. The signs of functional derangement of the acoustic labyrinth are of the first importance in such differentiation. The earliest test suggested to indicate changes occurring in the scala media was a test of diplacusis binauralis dysharmonica. Shambaugh suggested that the hearing of a given pure tone in the affected ear as of higher pitch than in the uninvolved ear was owing to edematous swelling of the tectorial membrane as such swelling added to the mass of the membrane and thus threw its response farther toward the basal coil. Although many observers have stated that in diplacusis binauralis dysharmonica, the tone may be heard as of either higher or lower pitch, this has not been our experience. We have found that this test is exceedingly unreliable in individuals who have not had some musical training, enough at least to be able to distinguish frequency from intensity. We have found many individuals with Ménière's disease who were unable to do this, and since the sound of the tuning fork was less loud on the involved side, they reported it as being lower in pitch. To us the statement that a sound may be heard at a lower pitch in the involved ear is the result of faulty observation. Therefore we believe the test for diplacusis is not dependable in distinguishing endolymphatic hydrops from other conditions in which unilateral loss of hearing may be associated with episodes of vertigo.

Fowler originally introduced the recruitment of loudness test as a means of distinguishing between early otosclerosis and nerve deafness. Dix, Hallpike and Hood and Dix suggested that the phenomenon is characteristically associated with pathologic processes involving the hair cells of Corti's organ and is characteristically absent in disorders of the cochlear nerve fibers.

Dix and Hood pointed out that full loudness recruitment may occur in 8 per cent of cases of VIII nerve tumors. This they attributed to changes in the hair cells resulting from interference with the blood supply to the cochlea. Hood has pointed out that the recruitment phenomenon is particularly subject to auditory fatigue, which he attributed to some failure of the capacity for energy restora-

tion in Ménière's disease. Thus in testing for loudness recruitment in Ménière's disease, the stimuli should be brief and intermittent.

With these two reservations in mind the test for recruitment of loudness is a dependable test in the differentiation of Ménière's disease from other types of episodic vertigo.

Carhart suggested use of the monitored live voice as a test of auditory acuity. Harris pointed out that a fallacy of the monitored live voice test was that equal intensity of two words at a meter is not necessarily the same thing as equal intelligibility at the brain. He suggested that recordings of the *Harvard Phonetically Balanced Lists* could be made so that representativeness and homogeneity of intelligibility will be secured.

Huizing and Reyntjes demonstrated that in addition to an articulation curve indicating loss of pure sensitivity and one indicating a combination of loss of sensitivity with loss of discrimination due to loss of perceptive hearing, there was a third characteristic articulation curve combining loss of sensitivity with loss of discrimination by preponderant subjective distortion due to recruitment. In this curve when the optional level is passed, the articulation score rapidly falls.

We have found severe loss of discrimination to be characteristic of the active stage of Ménière's disease, although in remission this test may not give particularly characteristic findings.

Bárány described the symptoms of a patient in whom severe vertigo and nystagmus were brought about when the patient was placed in a supine position with the head to one side. He noted that the nystagmus and vertigo disappeared rather rapidly if the critical head position was maintained. Bárány found no other evidence of ear disease and concluded that since the vertigo and nystagmus were brought on by position of the head in space the disorder was owing to a disturbance of utricular function.

Bárány also noted a positional nystagmus that tended to be maintained. Nylén found that in certain instances this nystagmus differed in direction with changes in position of the head and for that reason called it "direction-changing nystagmus." He found too that this type of nystagmus was not infrequently associated with

lesions of the posterior fossa. Lindsay also investigated positional nystagmus and concluded that it might be due to factors other than disease of the otoliths or central connections of the labyrinth.

Dix and Hallpike stated that in positional nystagmus, tests of cochlear and vestibular function (with the exception of the Nylén tests) give normal results. Evidence of aural disease, although present in some cases, is inconspicuous in most and entirely absent in more than a third. There are no associated neurologic lesions. Clinical examination in 100 cases supplemented by histologic studies in a single characteristic case led them to the conclusion of Bárány that disease of the otoliths is the cause.

McNally questioned this conclusion because experimental stimulation of the utricle does not produce nystagmus.

Utricular disturbance might better be hypothesized in a patient one of us (HLW) recently saw who reported recurring attacks of dizziness with a feeling of falling backward. Results of all vestibular tests except the Nylén test were normal. In the head-hanging position this patient had a severe subjective sensation of falling backward but there was no nystagmus of any kind.

Dix and Hallpike and Cawthorne, Dix, Hallpike and Hood also distinguished vestibular neuronitis which they described as a condition of vertigo, usually but not always paroxysmal, without cochlear signs or symptoms. They stated that vestibular neuronitis is due to some form of organic disease confined to the vestibular apparatus and localized in its peripheral pathways, central to Scarpa's ganglion up to and including the vestibular nuclei in the brain stem.

The Nylén test is a valuable differential test when vertigo, dizziness, or the like is a major complaint, particularly when nystagmus is present.

Vestibular function also may be tested by the Bárány caloric test or one of its modifications. We use a modification of the Kobrak test in which 5, 15 or 30 cc of ice water is injected slowly into the external auditory canal. Five cubic centimeters of ice water nearly always yields a minimal result and causes little discomfort for the patient. Whereas a hypoactive labyrinth is demonstrated no more than half of the time in Ménière's disease, this test is helpful in certain patients

who complain of vertigo or dizziness and in whom a hypoactive labyrinth is the only positive finding.

We have not found the directional preponderance test to have the value attributed to it by Cawthorne, Dix, Hallpike, and Hood. Anthony made extensive tests with this method and concluded, as did McNally and his co-workers,[32] that this was not a clinically useful test, principally because of the difficulty in obtaining an accurate end point. An accurate end point was found by Mahoney to be even more difficult to ascertain by electrical nystagmometry.

Last, but by no means least, physicians should remember Hoople's statement that examination of the pupils and ocular fundi, a test for facial and corneal anesthesia, a Romberg test, and a roentgenogram of the skull should be included among the practical labyrinthine tests. It is our belief that the great majority of the patients should have a complete neurologic examination.

THE DIAGNOSIS

If a carefully taken history is integrated with a series of carefully done tests of the labyrinth, it may be possible to conclude that the patient is suffering from Ménière's disease. The diagnosis cannot be made from the history alone or from the tests alone as a so-called typical history may be given for lesions other than end-organ lesions, and so-called typical findings on tests have been demonstrated in labyrinthine disorders following recovery from one of the viral diseases and have remained unchanged over many years.

CAUSES OF VERTIGO AND DIZZINESS

In 1954 McNally and Stuart reviewed 195 of 200 consecutive cases of vertigo which had been studied in 1949. They classified their cases into 21 groups on the basis of the causative factors as follows:

1. "True" Ménière's syndrome (endolymphatic hydrops)
2. Atypical Ménière's syndrome
3. Toxic labyrinthitis
4. Coronary thrombosis
5. Hypertension
6. Hypotension
7. Rheumatic heart disease

8. Arteriosclerosis
9. Coronary sclerosis
10. Posttraumatic vertigo
11. Brain tumor
12. Neurosyphilis
13. Cerebrovascular disease
14. Encephalomyelitis
15. Cerebral atrophy
16. Multiple sclerosis
17. Postinflammatory vertigo
18. Cerebellar artery syndrome
19. Neurologic lesion undiagnosed
20. Otosclerosis
21. Psychosomatic vertigo

Although this grouping is interesting, we have found it a little difficult to differentiate vertigo caused by coronary thrombosis, coronary sclerosis, rheumatic heart disease, hypertension, hypotension and cerebrovascular disease. Also the criteria that were used for the diagnosis of atypical Ménière's syndrome are not too clear. However, in none of the cases in which a diagnosis of true Ménière's disease was made in 1949 was the diagnosis changed in 1954.

In our own cases we decided that the primary distinction was between Ménière's disease and some other condition. The term "atypical Ménière's syndrome" can mean little else than not Ménière's disease and in our study we found no case that in our opinion did not fall into some other group.

Levy and O'Leary in discussion of the incidence of vertigo in neurologic conditions included platybasia and basilar impression as possible causes of vertigo associated with loss of hearing and listed Paget's disease as the most common cause of acquired basilar impression. They also included cerebellopontine angle tumors, epilepsy, migraine, and anxiety hysteria among the causes of episodic vertigo.

Alpers stated that recurring vertigo is an initial symptom in 10 per cent of the cases of multiple sclerosis.

Weiss pointed out that if the carotid sinus syndrome is mild, lightheadedness, weakness, dizziness and dimness of vision associated with nausea and vomiting, sensations which are often termed vertigo by the patient, may be present.

Many authors have pointed out that occlusion of the eustachian tube might produce some degree of vertigo. In fact Scott stated that in his experience Ménière's disease was simply unilateral eustachian

insufficiency. Robison stated that chronic congestion of the eustachian tube could result from inflammatory narrowing of the tubal lymph vessels secondary to infection in the adenoids, tonsils or paranasal sinuses.

Shield concluded that the dizziness and even vertigo which he often found associated with myxedema were due to occlusion of the eustachian tube by swollen mucous membranes. Athens reported on 30 patients with hypometabolism who were subject to recurring attacks of true vertigo. It seemed to him that the tendency to retain water in thyroid deficiency might lead to hydrops of the labyrinth. He did not indicate how endolymphatic hydrops might produce vertigo without affecting the hearing. It seems probable that Shield's explanation is the better one.

Certainly central vascular disease should be considered in the differential diagnosis of vertigo if only because Ménière wrote his original papers for the purpose of differentiating a distinct group of individuals with vertigo from apoplectiform cerebral congestion. Millikan and Siekert found 13 of 20 patients with verified thrombosis of the basilar artery had complained of vertigo and Siekert found that 12 of 33 with tumors of the glomus jugulare had vertigo.

Bruns' syndrome, originally described as episodic attacks of nausea and vomiting associated with cysticercocis of the fourth ventricle, should be included because of the dramatic nature of the attacks which have frequently been diagnosed as Ménière's disease before the development of functional testing of the labyrinth.

Lindsay and Hemenway have described vertigo from labyrinthine hypoactivity.

MATERIAL STUDIED

In the preparation of this paper the case records of all patients who gave vertigo or dizziness as a major complaint at the Mayo Clinic in the year 1954 were studied. There were 632 such patients. In addition the records in 50 unselected cases of multiple sclerosis and 66 cases of tumor of the posterior fossa encountered in 1954 were studied for the symptom of vertigo or dizziness.

TABLE I

CASES OF VERTIGO GROUPED ON BASIS OF ETIOLOGIC FACTOR

Ménière's disease	111
Possible Ménière's disease (diagnosis inconclusive)	5
Vertigo on movement*	94
Vertigo from position of head*	32
Motion sickness	2
Toxic labyrinthitis	60
Carbon monoxide poisoning	3
Vestibular neuronitis	3
Utricular	2
Labyrinthine hypoactivity	19
Posttraumatic vertigo	22
Syncope	4
Hyperactive carotid sinus	1
Neurocirculatory asthenia	20
Lesion of the central nervous system (probably vascular insufficiency)	34
Multiple sclerosis	3
Brain tumor	5
Degenerative disease of brain stem or cerebellum	2
Convulsive disorders	10
Migraine equivalent	2
Vascular accident labyrinthine artery	23
Basilar artery syndrome	2
Hypertension and cardiac disease	51
Tubal occlusion	6
Post-measles vertigo	3
Polycythemia vera	1
Episodic vertigo after radical mastoidectomy	4
Vertigo with diplopia (episodic)	3
Nasal polyposis	1
Syphilis	6
Dizziness (cause undetermined)	14
Psychosomatic vertigo	49
Chronic otitis media, bilateral (episodic vertigo)	1
Weakness or unsteadiness	2
Vertigo (cause undetermined)	32
Total	632

* See Tables II and III for further details of cause of vertigo.

FINDINGS

The 632 cases were divided into the 34 clinical groups on the basis of diagnoses as shown in Table I. Since all but one of these patients were alive, the diagnoses cannot be considered exact and may well be challenged. We believe, however, that the differentiation of Ménière's disease from other forms of vertigo and dizziness is definite and conclusive in all but five of the cases studied. It can be seen, therefore, that Ménière's disease was present in about a sixth of our cases in which the major complaint was vertigo or dizziness. No patients given a diagnosis of vertigo as being due to platybasia, basilar impression or Bruns' syndrome were encountered in 1954, although cases of both types have been seen in past years.

TABLE II

AGE DISTRIBUTION FOR MÉNIÈRE'S DISEASE*

YEARS	NUMBER	PER CENT
10 - 19	1	0.9
20 - 29	3	2.7
30 - 39	21	18.9
40 - 49	31	27.9
50 - 59	35	31.6
60 - 69	18	16.2
70 - 79	2	1.8
Total	111	100.0

* The youngest patient was 16 years, the next two youngest were 25 and 28 years.

Of the 111 patients in whom a diagnosis of Ménière's disease was made, 72 (64.9 per cent) were males, and 39 (35.1 per cent) were females. That Ménière's disease is a disorder of the middle-aged is shown in Table II. All but six of the patients were between 30 and 70 years old.

The difficulty we encountered in making a diagnosis in some of our cases is indicated by the fact that a complete neurologic examination was required to establish the diagnosis of Ménière's disease in 45 (40.5 per cent) of our 111 cases.

TABLE III

EPISODIC VERTIGO FROM CIRCULATORY DISORDERS: INCLUDED AMONG THE CIRCULATORY DISORDERS ARE HYPERTENSION, CARDIAC DISEASE, NEUROCIRCULATORY ASTHENIA, VASCULAR INSUFFICIENCY, VASCULAR ACCIDENT AND BASILAR ARTERY SYNDROME

AGE GROUP	NUMBER	PER CENT
10 - 19	3	2.3
20 - 29	2	1.5
30 - 39	7	5.3
40 - 49	21	16.1
50 - 59	46	35.1
60 - 69	36	27.5
70 - 79	16	12.2
Total	131	100.0

Since the group of patients with episodic vertigo from circulatory disorders is slightly larger, it was felt that their age distribution might be of interest (Table III). All but 12 of these patients were between the ages of 40 and 79 years. Although this is a somewhat older group than that with Ménière's disease, the difference is not sufficiently great to be helpful in diagnosis.

As can be seen, we have had some difficulty in making the diagnosis of vestibular neuronitis so favored by Cawthorne and his associates.[8,9] It is probable that they would have included many cases in the group of vertigo from change in head position in this category. However, they thought that patients with vestibular neuronitis tend to recover in a year or less and most of our patients had had vertigo for a much longer period without any tendency to alleviation. In addition, as we stated previously, McNally has cast doubt on their assumption that this symptom is due to utricular disturbance and we are inclined to think that McNally, with his extensive physiologic background, is probably correct. For this reason, we attempted a further breakdown of cases in which head position was associated with vertigo (Table IV).

It may be of interest that whereas nearly a third of the patients on whom a Nylén test was done showed position changing nystagmus, none of them gave evidence of disease of the central nervous system (Table IV) on complete neurologic examination usually including an electroencephalogram.

It was thought that a breaking down of the cases of vertigo on sudden motion of the head or body would be of interest (Table V). This table, however, indicates little more than the difficulty in selecting a basis for the symptoms.

TABLE IV

VERTIGO ON POSITION OF HEAD

		CASES	PER CENT
Cause indeterminate		15*	46.9
CNS arteriosclerosis		3	9.3
Nylén test positive		14	43.8
Type 1	10		
Type 2	4		
Total		32	100.0

* The cases termed indeterminate did not have Nylén tests performed.

In 19 of our cases the only positive finding that could be suggested as a cause for recurring vertigo was unilateral or bilateral labyrinthine hypoactivity (Table VI) as suggested by Lindsay. Our cases of vertigo indicate that both unilateral and bilateral labyrinthine hypoactivity produce episodic vertigo. This group points up the need for caloric testing in all patients with a complaint of vertigo, dizziness, or the like.

In our group of 50 cases of multiple sclerosis only the two patients who had episodic vertigo could be considered as having vertigo, dizziness and the like as an initial expression of multiple sclerosis. In the other patients these symptoms were incidental and were brought out only on questioning (Table VII). Alpers, as mentioned earlier, had stated that 10 per cent of the patients with multiple sclerosis had vertigo as an initial episode.

TABLE V

PRINCIPAL COMPLAINTS OF
VERTIGO ON MOTION OF HEAD OR BODY

	CASES
Cause indeterminate	45
Vascular insufficiency of the central nervous system	34
Toxic labyrinthitis	5
Latent syphilis (question of neurosyphilis)	4
Hypoactive labyrinth	1
Menopause	1
Possible acoustic neuroma	1
Anemia	1
Dizziness on effort	1
Psychogenic vertigo	1
Total	94

TABLE VI

VERTIGO WHEN HYPOACTIVE LABYRINTH
IS ONLY POSITIVE FINDING

HYPOACTIVE LABYRINTH	CASES
Bilateral	7
Unilateral	12
Total	19

Since the incidence of vertigo in lesions of the posterior fossa has been of interest, all the cases in which a definite diagnosis of lesions of the posterior fossa was made during the year 1954 were reviewed. In approximately a quarter of these, vertigo was a major complaint and in an eighth, motion within the head was a major complaint (Table VIII).

TABLE VII

VERTIGO IN 50 UNSELECTED CASES OF MULTIPLE SCLEROSIS: ENCOUNTERED IN 1954

	CASES	PER CENT
No vertigo, dizziness, or similar complaint	39	78
Dizziness	4	8
Vertigo (episodic)	2	4
Vertigo or dizziness on change of position	5	10
Total	50	100

TABLE VIII

VERTIGO ASSOCIATED WITH TUMORS OF THE POSTERIOR FOSSA IN YEAR 1954

	CASES	PER CENT
No vertigo or dizziness	42	63.6
Dizziness (not vertigo)	8	12.1
Vertigo	16	24.3
Total	66	100.0

COMMENT

Vertigo and dizziness seem to be important symptoms since more than 600 patients gave them as a major complaint during the course of one year at the Mayo Clinic.

The fact that a sixth of these patients were given a diagnosis of Ménière's disease not only indicates the importance of this disease in the production of the symptom of vertigo but also the care which must be taken to differentiate it from other disorders that might tend to masquerade as Ménière's disease.

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LXV

OTOSCLEROSIS IN TEN PAIRS OF IDENTICAL TWINS

A CONTINUING STUDY

EDMUND PRINCE FOWLER, M.D.

NEW YORK, N. Y.

Our knowledge of the etiology of otosclerosis (otospongeosis) is meager. Even this is an understatement. However a paucity of knowledge should not deter discussion of a mystery. It should on the contrary spur us on to further search for some factor in the biological or social environment present in all instances which might supply a key to the true etiology.

The more pertinent facts at our disposal have been those concerning heredity and the incidence of occurrence in whites and negroes and the sex ratio, as so definitely revealed by Stacy Guild's autopsies reported in 1944.[1]

Unfortunately neither histopathologic statistics nor animal experiments have shed any light on the etiology of otosclerosis. Clinical investigation seemed the most promising line of attack. (It seems to have proved so to be.)

Identical twins (monovular) (monozygotic) originate in the same egg (the same zygot) and therefore have a similar hereditary background not only for bodily appearance, but for tendencies to acquire similar diseases and disorders of body and mind, especially if they live together in a similar environment.

The two ears of any individual also are twins, as are the two sides of the body. Also they are subject to hereditary and environmental factors in much the same way as identical twins. They, too, definitely come from one egg and like many twins are mirror images of one another. Like the twins they often differ considerably in

size, form, function and predilection to certain disorders, one of which is otosclerosis. Their vascular trees though usually similar may differ much in distributory details.

In each pair of twins we have one body (the egg) developing into two bodies, and so we are furnished with a unique control. In fact no better control can be imagined for clinical studies of humans. You may remember the story about the psychologist who had one of his twins baptized and used the other for a control.

When differences can be found in identical twins they should be studied with a view to linking them with variations in the timing and intensity of various environmental factors. For this reason I have been studying identical twins one or both of whom have acquired otosclerosis in one or both ears. Some of the findings are interesting.

It is difficult to obtain many identical twins who have deafness from otosclerosis. It has been difficult to find identical twins with only one of their ears deafened by otosclerosis, and still more difficult to discover twins one of whom had no deafness and the other definite progressing deafness from otosclerosis.

Fortunately during the past 18 years I have managed to examine repeatedly ten pairs of twins several of whom revealed these differences.

I obtained most of my twins through the New York League for the Hard of Hearing. Although letters were sent to all otologists in North and South America, Africa, Australia, China and Europe I received only a few responses, none of which could be used because the twins had not been studied or were not available for sufficiently detailed study to be included in the group herein discussed.

It seemed advisable to start observation when the twins were young. This I tried to do by examining over 200 pairs of twins obtained through the public schools in New York City. Unfortunately for me (but not for the twins) I found not a single twin who showed a deafness which could be diagnosed "otosclerosis." This was not unexpected because the twins were under 15 years of age. Moreover owing to changing domiciles few follow-ups were possible.

Also some years ago in two elementary schools of over 1,000 pupils each I found no child having otosclerosis.

In my otosclerosis file (over 1,000 histories) there are only 12 children under 15 years of age diagnosed otosclerosis, and in all of these a question mark is affixed. Only when there is a progressive deafness without any suspicion of a complicating recurrent impedance lesion and no neural deafness affecting the lower frequencies should we make a definite diagnosis of otosclerosis in children under 15 years of age.

Incidentally I examined 100 hard of hearing school children of like ages to the twins and found only one instance of otosclerosis[2] and this was questionable. There are no criteria for the early diagnosis of otosclerosis because if deafness occurs it is a late result of the lesion.

In the study of twins before all else it was necessary to be quite certain that the twins were identical. This was determined from reports of the accoucheurs, by photographs of the right, left and full face, and by finger and palm prints of both hands. Many almost unbelievable similarities were observed. The geneticist, the late Dr. Charles Davenport, aided and encouraged me in these studies.

So much data have been accumulated that to put it all in tables would be redundant, and as much of it seems at this time to be statistically of little or no value I will merely set forth in more or less chronological order the sequence of our clinical approach and then, to avoid unnecessary repetition, discuss what appears to me to be the most pertinent findings in each area of investigation.

AREAS OF INVESTIGATION

Heredity. Six pairs of twins had definite family histories of deafness; in four, a family history of deafness was uncertain or unobtainable. Of the six positive histories one pair (No. 9, Table I) had both maternal and paternal histories of progressive deafness; two pairs had a maternal history (Nos. 3, 10) and three pairs had a paternal history (Nos. 4, 6, 7). There was no deafness from otosclerosis in any of the older or younger siblings.

TABLE I

PAIR NO.	TWIN	AGE OF PUBERTY	INTERVAL IN YEARS	AGE DEAF-NESS FIRST NOTED	TWIN	AGE OF PUBERTY	INTERVAL IN YEARS	AGE DEAF-NESS FIRST NOTED
Females								
1	A	15	3	18	**B**	14		12
2	A	16	1	17	**B**	14½	5	20
3	**A**	13	7	20	B	14	6	20+
4	A	14.1	14	R. none L. 28	**B**	14	9	23
6	**A**	12	5	17	B	12+	5	17+
7	A	14	19	R. none L. 33	**B**	13	15	28
8	A	17	16	R. none L. 33	**B**	15	13	28
9	**A**	14	3	17	B	14.1	?	7?
Males								
5	A	15	19	34	**B**	15	4	19
10	A	15	5	R. none L. 20+	**B**	15	5	20

Bold letter indicates the deafer of the twins at the first examination.

COMMENTS

No two people stabilize more evenly than twins, their bodily appearance and psychology are usually remarkably similar. However identical twins may react differently even to similar environment. In this connection it should be realized that although originally little or no divergencies may appear in twins, inevitably and progressively somatic and psychological divergencies appear and tend to increase during life.

In three pairs (4, 7, 8) neither parent had any deafness and these pairs acquired deafness when much older than any of the other

female twins. In all three twins A developed no deafness until about 30 years of age and then in only one ear.

Hereditary disorders often may not reveal themselves for one or several generations. Human beings do not propagate as do flowers or rabbits and there may be no sign of hereditary disease for several generations unless dominant genes are present in both parents. But the tinder is there and it may require but a little spark to kindle it. It did so in these three pairs but only in one ear and the spark was emotional strain.

Keep in mind that otosclerosis can be present with no impedance deafness unless the lesion is extensive enough to involve the annular ligament.

MOTHER'S HISTORY

Health During Pregnancy. Numbers 1, 7, 10 very ill with nausea and vomiting, nephritis and hypothyroidism respectively.

Diet During Pregnancy. Six satisfactory; three unsatisfactory; one mostly milk and ice (account of nausea and vomiting), one no meat or salt (nephritis), one hypothyroidism. (These were the three very sick mothers.) Diet not known in mother of one pair.

Exanthemata. None were reported during pregnancy of any of the mothers.

Labor. Difficult in three instances.

Lactation. Three pairs of twins were nursed for three months and one of these pairs for an additional two months (half breast fed and half bottle fed because of scanty milk); one pair nursed one month; six pairs not breast fed.

Drugs Taken. In seven no medication; three uncertain.

Siblings Born Before and After the Twins. In five pairs one to nine siblings were born before the twins, and in these five pairs in only one were siblings born after the twins (two). In three pairs none were born before and only one was born after in each pair. In two pairs none were born before or after.

COMMENTS

In only four pairs were there siblings born after the twins and in only one of these pairs were as many as two born after the twins. In several hundred non-twin siblings I have found that in large families (5 or more siblings) the incidence of otosclerosis was definitely higher in the younger siblings than in the middle and older siblings,[3] whereas in the smaller families it was higher in the older siblings. Sex and order of birth of siblings entail environmental differences. These may be sufficient to influence the acquisition or timing of the acquisition of the lesion.

SIMILARITIES AND DIFFERENCES

Weight at Birth. Weights were similar in three pairs; in two pairs the weights were unobtainable; in five pairs the weights differed one-half pound and in four of these the heavier twin was first born.

Living Proximity. In nine instances the twins slept in the same bed for many years. In this respect the early environment was therefore quite similar.

Allergies. Although in a few pairs one or both twins gave a history of allergic reactions to a wide variety of allergins no significant correlations with the date of onset, rate of progress, degree of deafness or date of stabilization could be found. One individual had migraine, and she was the deafened twin whereas her less emotionally sensitive sister had no hearing loss.

Head Colds. Six pairs had few; three pairs A more than B; one pair B more than A.

Tonsillectomy and Adenoidectomy. In eight pairs both twins had a tonsillectomy and adenoidectomy and in one of these pairs one twin had two tonsillectomy and adenoidectomy operations; in one pair only one twin had a tonsillectomy and adenoidectomy; in one pair neither had a tonsillectomy and adenoidectomy.

Hypertrophied Lymphoid Tissue. In three pairs (4, 5, 6) at the time of my first examination it was normal. In three pairs (1, 3, 7)

there was more lymphoid tissue in the deafer twin; in one pair (2) there was more lymphoid tissue in the better hearing twin; in three pairs (8, 9, 10) it was moderate but not noticeably different.

COMMENTS

It would appear that none of these factors exerted a controlling influence upon the etiology or course of the otosclerosis.

Diseases of Childhood: Exanthemata. Nine pairs gave a similar history with one exception in which only one twin had mumps. In one pair Twin B had "everything" whereas Twin A had only measles and scarlet fever.

Diet. In three pairs one twin drank more milk, in two pairs one ate more fruit. When one twin had more coffee, milk, fruit, the difference in diet did not appear to correlate with the priority of date of onset of the deafness or its relative severity.

Teeth. In pair 1 both had five extracted in their teens, A had less cavities and less deafness. In pair 2 all teeth have required filling in A and many in B, the more deaf. In pair 3 casts showed mirror images of conformation and of cavities. In pair 4 both had several extractions. In pairs 5, 10 (males) both twins in both pairs had good teeth. In pair 6 both have very soft teeth. In pair 7 both have similar hard teeth. In pair 6 both have very soft teeth. In pair 7 both have similar hard teeth. In pair 8 A had soft teeth and less deafness than B who had hard teeth. In pair 9 both had much dental work; A, the deafer, had less.

Tinnitus. In four pairs (1, 3, 6, 8) both twins had tinnitus. In five pairs (2, 4, 5, 7, 9) one twin had tinnitus and in four of these pairs (2, 4, 7, 9) the twin with tinnitus was the deafer. In one pair (5 male) the twin without tinnitus was the deafer. In one pair (10 male) neither had tinnitus. In pairs 4, 7, for several years one of the twins in each pair did not reveal any deafness and never tinnitus in either ear but the deafened twin sister had tinnitus, and was the more emotionally labile.

Smoking Habits. In one pair both smoked a pack of cigarettes a day. In one pair both seldom smoked. In six pairs neither smoked.

In one pair **A**, the deafer, seldom smoked and B smoked a pack a day. In one pair **A**, the deafer, never smoked and B smoked some.

COMMENTS

There appeared to be no relationship between the diseases of childhood, dietary habits, the degree of hardness of the teeth nor between smokers and nonsmokers in the priority or severity of the deafness. However excessive smoking if it accentuated emotional episodes conceivably might be given consideration. As is usual the tinnitus was associated with emotional hypersensitivity.

Otoscopy. Was within average normal variations except in twin B in pairs 8 and 9 in whom dullness of the drum was noted.

Earaches or Discharge. None in six pairs; in one pair (6) both in infancy; in one pair (7) A negative, B at 19; in one pair (8) A at 12 and B at 2; in one pair (9) A at 9 and B at 7 and 9. No chronic suppurative otitis in any of the twins; no external otitis; no ear operations.

Blood Pressure. With the exception of both twins in two pairs in which it was low the resting blood pressure was within average normal range.

Menopause. In one pair of twins the menopause in both A and B occurred at the age of 48 years (pair 2). All of the other twins were well below the usual menopause age.

Joint or Muscle Pains. All of the twins were free of bone or joint disorders with the exception of one twin (pair 2, B) who suffered a fracture of the shoulder and pair 3, both of whom had growing pains and one (B) transitory muscle spasm.

Laboratory Examinations. Five years ago I published details of the laboratory findings and will omit them herein because they are as of now of little or no use statistically. They did demonstrate the remarkable ability of the blood to remain stable even in the presence of a bone dyscracia. In all but two pairs of twins the BMR, cholesterol, calcium, phosphorus and phosphotase determinations, blood counts, differentials and hemoglobin were remarkably similar.

Hearing Aids. Pairs 1, 4, 5, 8, 10 neither twin wore a hearing air; (pairs 1 and 10 both should use an aid; pair 8 B should use a hearing aid; pairs 4 and 5 each has good hearing in one ear.) Pairs 2 and 7, one wears a hearing aid (pair 2, both should wear an aid; pair 7, A has average normal hearing in right ear); pairs 3, 6, and 9, both wear a hearing aid.

Hearing Levels. Over a long period of years the hearing changes may be summarized as follows: When the hearing at the first examination was down 50 db or more, in only one pair did the impedance deafness markedly increase (more than 15 db) on subsequent examinations. This suggests that in the severely deafened twins there was a remarkable tendency to stabilize the stapes impedance. It may well be that when the lesion caused about a 50 db loss a greater impedance was impossible at the site of the annular ligament and no involvement of the round window had occurred. Plus and minus fluctuations of 5 and even 10 db were frequent between the yearly or more frequent tests.

The bone coduction was normal or near normal except for the higher frequencies in the two older pairs of twins. It was interesting that in five pairs the deafer ear in one twin was the better ear in the other. In five pairs the deafer and the better ears were on corresponding sides of the heads.

Age of Puberty, Age Deafness First Noted (or Admitted) and Time Between (Table I). In the sixteen females in two instances (3, 9) puberty was first attained in Twin A; in five pairs (1, 2, 4, 7, 8) it was first attained in Twin B; in one pair (6) at about the same age.

There were seven pairs (1, 2, 4, 5, 7, 8, 9) with difference in dates of onset of deafness. In all but one (2) the first to notice deafness from the otosclerosis remained the deafer twin.

I am of the opinion that when the deafness was not admitted until after 20 years of age it had existed to some degree for some time before 20 years of age.

With two exceptions (one twin in pair 1 and both twins in pair 6) puberty occurred later than average. In females the average age

of puberty is 12 years, in the men 15 years was taken for the age of puberty. They appeared to be retarded in this respect.

Twin B in pair 1 noted deafness in left ear before puberty. There was a history of left earaches and I doubt if this early deafness was due to otosclerosis. Twin B in pair 9 had a nonprogressive deafness from otitis media in infancy. These were the only twins to acquire deafness in either ear before puberty. The age of puberty, per se, did not appear to correlate with the age deafness appeared.

The interval between the age of puberty and the age of deafness in eight pairs of twins varied from 1 to 9 years. In one ear in one of the males (A in pair 5) it was delayed until 19 years after puberty; in pair 7 it was delayed for 19 years in A and 15 years in B; in pair 8 it was delayed for 16 years in A and 13 years in B. In all but two individuals (B in 1 and A in 2) deafness was delayed until 3 or more years following puberty. In 3 pairs (4, 7, 8) the onset of deafness in one or both ears was late (well after 20 years of age). In these 3 pairs deafness ultimately developed in Twin A in one ear only. In 7 of the 10 pairs deafness occurred before 21 years of age, in one or both twins of a pair, and ultimately in both ears with one questionable exception (A in 10).

Marriage. When first examined in 3 pairs (5, 6, 9) both were married; in 1 pair (8) one was married but subsequently her twin spinster sister married, and in 2 pairs (1, 4) both subsequently married. In 3 pairs neither have married (3, 7, 10). In pair 2 only twin B is married.

Children Born to Twins and Effect of Childbirth on Hearing:
PAIR 1: A 5 children, **B** 1 child.

A, after birth of first child in the right ear no change at 1000 but a varying loss at the other frequencies in the right e ar. In the left ear (the worse ear) no significant change. After the birth of the fifth child, in the right ear there was a loss in the different speech frequencies varying from 10 to 40 db and in the left ear a loss of 10 to 15 db.

B, soon after birth of only child, showed no significant additional loss in either ear. However during the next five years both ears

showed a further loss of 5 to 10 db. (Husband had been killed in the war three months after birth of baby.)

PAIR 2: A unmarried, **B** 2 children.

Not examined before she bore the children.

PAIR 3: Both unmarried.

PAIR 4: A 3 children, **B** 4 children.

A, (first examined in 1946, married in 1947 average normal hearing in both ears until one month subsequent to birth of first child (August 1948) at which time the hearing in the right ear was still average to high normal at all frequencies and in the left ear also, above the 500 frequency. However, in the left ear at 250 the threshold was now 20 db which was a 10 db increase in loss from one year previously. The second child was born one year later (1949) and the hearing in the right ear showed no change; the hearing in the left ear showed a further loss of 5 to 10 db but only at the lower frequencies. After the birth of the third child (3 years later) the right ear still maintained average to high normal hearing and the left ear showed a further loss of 10 to 15 db at the low and more important speech frequencies. A year later the right ear showed a loss of 10 to 15 db in the two lower frequencies and the left ear showed a 5 db loss in the middle frequencies and a 15 db loss at 125 bringing the hearing down to a level of 60 db for the two lower frequencies and 30 to 40 db for the middle frequencies.

(NOTE—After 11 years the right ear shows only a slight loss of 5 db at 500 and 15 db at 250; in the left ear the hearing had gone down slowly throughout this period reaching a level of loss at the middle and lower frequencies of from 30 to 60 db.)

B, (first examined in 1946, married in 1952) the right ear revealed a loss of 10 to 15 db in the middle frequencies and 20 to 25 db in the two lower frequencies. The left ear was average to high normal.

(NOTE—Mirror images to twin A.)

Both ears, following emotional episodes one and a half years later showed an elevation of the hearing threshold of from 5 to 20 db at the lower frequencies. During the following 5 years there was no further significant change in the hearing at any of the frequencies in either ear, nor in 1953 before or following the birth of B's first child. The second child was born in 1954 and unidentical twins in 1956. This patient has been too sick to be examined during the past two years but she reports a further loss of hearing.

PAIR 5: (males) A 2 children, **B** 1 child.

PAIR 6: **A** 3 children, B 4 children.

The hearing in both ears of both twins was 40-50 db down in the lower frequencies and showed only a 5 to 10 db further loss on subsequent examinations.

PAIR 7: (Unmarried to date.)

Divorce of parents caused more emotional repercussions in Twin **B** than in Twin A.

PAIR 8: A 4 children, **B** 2 children.

A, right ear average to high normal, left ear likewise in middle and high frequencies but 15 to 20 db down in the three lower frequencies. There was a 5 db further loss only in the two lower frequencies in the left ear on subsequent examinations.

B, before marriage the loss in the right ear was 25 to 40 db in the middle and low frequencies, and in the left ear 40 to 45 db in the lower frequencies and 60 to 65 db in the middle frequencies. There was a severe loss for the frequencies of 4000 and 8000 in both ears. Subsequently during two pregnancies (1953 and 1955) there was little or no further loss in either ear. In 1957 there was a further loss in the lower frequencies of 5 to 10 db in both ears.

PAIR 9: **A** 2 children, B 1 child.

Not seen until after the birth of their children, but the deafness occurred long before they married.

A, the loss in the right ear was 50 to 60 db, and in the left ear 10 to 15 db less. The last test (1957) showed no further loss in the middle or high frequencies in either ear but approximately a 10 to 30 db further loss in the lower frequencies in both ears.

B, the right ear showed a 40 db loss in the four lower frequencies and a 15 to 30 db loss in the middle and high frequencies. In the left ear there was a 5 to 15 db greater loss, but in both ears during twelve years there was no more than a 15 db further increase in the deafness in either ear at any frequency.

PAIR 10: (Unmarried to date.)

COMMENTS

It will be noted that frequently there was no increase in deafness soon following the birth of a child, and that when it did increase it did not always occur in both ears. Moreover it was usually delayed for a considerable time, over a year, unless some emotional strain also occurred. Many of the children born to these twins have been examined. None revealed otosclerosis. However some are approaching puberty and I plan follow-ups whenever possible.

BLUE SCLERAE AND EMOTIONAL LABILITY

A noticeable increase in the blueness of the sclera was generally observable near the onset of menstrual periods with no immediate effect upon the hearing. Also this has been observed in non-twins with deafness from otosclerosis, and as in these twins has been associated with emotional factors.

At the time of the first examination in five pairs (1, 4, 7, 8, 10) the deafer twin was the more emotional and had the bluer sclera except in one instance (7) where the degrees of blueness were at times identical but varied from 0 to 1 or 2 plus.

At the first examination in pairs 2 and 3 the less deafer twin was the more emotional and had the bluer sclera. In pair 5 in both twins the sclerae were white. In pair 9 in both twins the sclerae were of equal blueness.

Pair 6 were not seen until aged 38 years. The sclerae were then white in both. Both had been highly sensitive emotionally.

With the exception of pairs 5, 6 and 9, the degree of blueness of the sclerae was observed to vary considerably, and as between A and B.

INTRAVASCULAR AGGLUTINATION OF THE BLOOD ("SLUDGING")

In five pairs (2, 3, 4, 8, 10) the twin with the greater degree of blueness of the sclera revealed a more marked degree of sludging. When the sludge was marked in both A and B the more emotional of the pair usually had the bluer sclera.

In pair 9 sludging was marked in both A and B and the sclerae were one to two plus in both; B was the more emotional.

COMMENT

In six pairs (2, 3, 4, 7, 8, 10) the sludging was definite and more marked in the more emotional twin and the twin with the bluer sclera. It will be noticed that in these six pairs there appeared to be a definite correlation between sludging, emotional sensitivity and blueness of the sclera.

SUMMARY AND CONCLUSIONS

I have set forth my observations on the internal and external environment of ten pairs of identical twins. In several there is established a consistent relationship to factors affecting the timing, prevention, genesis, or course of the deafness from otosclerosis.

It is remarkable that in every pair with two exceptions the twin who first developed deafness from otosclerosis was the twin who matured first, and who was subjected to the more marked emotional disturbances near pubescence. These emotional disturbances were usually associated with the death of a loved one, divorce, unhappiness in the family, severe illness, or frustrations of various kinds. They regularly preceded any evidence of deafness by several years.

I had found these factors to be important in nontwin siblings, but in such both heredity and environment are in many ways more variable, particularly because of differences in sex, in age of the siblings, and in age of the parents.

In identical twins any divergence in the functioning in any organ will be more disturbing to the twin who is the more precocious. The more mature takes on the care of the less mature of the pair and is therefore placed under more emotional strain than if both twins had matured equally. Interdependence is no longer so similar.

The absence of deafness does not necessarily imply the absence of otosclerosis. In four instances the normal hearing twin subsequently developed monaural otosclerosis.

This indicates that if one identical twin, or if one ear of any individual, develops otosclerosis the other twin or the other ear harbors it although it may be subclinical for a long time, even for a lifetime.

Since deafness from otosclerosis rarely if ever appears before puberty all children, especially females with positive hereditary histories, should be examined carefully before puberty approaches and measures taken to diminish or remove any factors which might even theoretically play a part in its genesis.

Although no mechanical or medicinal treatment appeared to have improved the hearing in these 20 individuals unless it was lowered by lesions other than otosclerosis, in a few instances deafness was delayed, and in several instances has not developed in the normal hearing ear of the individuals who ultimately developed a monaural deafness from otosclerosis. Something prevented or delayed the lesion. Several such results seem to be encouraging, to be more than mere happenstance.

In these twins there was a close correlation between hyperemotional sensitivity and the priority of onsets of puberty, and of the deafness, and the lesser time lags between these factors. This correlation strengthens the opinion that emotional strains with the hormone and neurovascular disturbances correlated therewith are important factors in the timing, genesis and exacerbations of the bony dyscracia known as otosclerosis, that they in fact trigger the faulty bone metab-

olism which is the operating factor in the genesis of otosclerosis in predelective individuals. This opinion is further strengthened by the observation that an increased hearing loss (an exacerbation of the lesion) seemed to be preceded by emotional strains whereas during even long emotionally quiet periods no increase in deafness took place. My conclusion is that continuing research gives more and more promise of proving my thesis, and of providing us with means to stop, delay and even to prevent crippling deafness from otosclerosis.

140 East 54th Street

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Notices

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY HOME STUDY COURSES

The 1958-1959 Home Study Courses in the basic sciences related to ophthalmology and otolaryngology, offered as a part of the educational program of the American Academy of Ophthalmology and Otolaryngology, will begin on September 1 and continue for a period of ten months. Detailed information and application forms may be secured from Dr. William L. Benedict, the executive secretary-treasurer of the Academy, 15 Second Street, S.W., Rochester, Minnesota. Registrations should be completed before August 15.

TEMPLE UNIVERSITY SCHOOL OF MEDICINE AND HOSPITAL

Postgraduate Course in Broncho-Esophagology February 16th to 27th, 1959.

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These courses are to be given in the Department of Laryngology and Broncho-Esophagology, Temple University Medical Center, under the direction of Drs. Chevalier L. Jackson and Charles M. Norris.

The tuition fee for each course is $250.00. Application blanks and further information concerning dates of subsequent courses may be obtained by writing to: Jackson-Research, Lab 604, Temple University Medical School, 3400 N. Broad Street, Philadelphia 40, Pa.

TEMPLE UNIVERSITY

There will be a postgraduate course in Bronchoesophagology November 3 to 14, 1958, and a postgraduate course in Laryngology and Laryngeal Surgery December 1 to 12, 1958, given in the Department of Laryngology and Bronchoesophagology, under the direction of Drs. Chevalier L. Jackson and Charles M. Norris.

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AMERICAN ASSOCIATION FOR CLEFT PALATE REHABILITATION

The American Association for Cleft Palate Rehabilitation will hold its 17th Annual Convention at the Sheraton Hotel in Philadelphia on Thursday, Friday and Saturday, April 30, May 1 and 2, 1959.

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AMERICAN LARYNGOLOGICAL ASSOCIATION

Copies of the Transactions of the American Laryngological Association are available for general distribution at $8.00 a copy. Please send request with check to Dr. James H. Maxwell, Editor, Transactions, Out-Patient Bldg., University Hospital, Ann Arbor, Mich.

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